

Healthline with Yale Cancer Center

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WTIC Newstalk 1080

Treatment Advances for Brain Tumors

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This is Healthline, a joint venture of WTIC NewsTalk 1080 and Yale Cancer Center. Yale Cancer Center is a resource for cancer programs throughout Connecticut, developing new advances in prevention, screening, diagnosis and treatment. On Healthline you will hear from some of the leading doctors in the country. Healthline is not intended to provide medical advice. Yale Cancer Center urges you to consult with a qualified physician in your community for diagnosis and for answers to your medical questions. And now, our co-hosts oncologists Ken Miller and Ed Chu

Chu Good morning and welcome to Healthline. My name is Dr. Ed Chu and I am Chief of Medical Oncology here at the Yale Cancer Center in New Haven. My co-host Dr. Ken Miller is still away on a well-deserved vacation with his family in Barcelona, Spain. Healthline, with the Yale Cancer Center, is our way of providing you with the most up to date information on cancer care every Sunday morning at 8:30 a.m. here on this station WTIC NewsTalk 1080. Our Healthline program features some of the nation's leading oncologists and cancer specialists who are on the forefront of the battle to fight cancer right here in our state of Connecticut. Each week we are joined by a different expert from the Yale Cancer Center and together we discuss the myths about cancer, the latest treatments available to cancer patients, and advances in clinical research. Our goal is to give you help and hope. We will answer your questions and provide you with the latest information on cancer. If you would like to submit a question about cancer to Healthline, please e-mail us at Healthline@Yale.edu or call 1-888-234-4-YCC and we will try to answer your questions on air in a future broadcast. If you are interested in listening to past editions of Healthline, or if you would like to learn more about a specific kind of cancer, all of our shows are now posted in both audio and written formats under the Yale Cancer Center website at www.yalecancercenter.org. Today our program focuses on the treatment advances in brain cancer and our special guest today is Dr. Joachim Baehring, Assistant Professor of Neurology and Medicine in Medical Oncology at the Yale Cancer Center. Joachim, thanks so much for being with us today on Healthline.

Baehring Thank you Ed, it is a pleasure to be here.

Chu Let us begin with a quick overview. What is brain cancer? As I understand there are many different types.

Baehring Yes, there are two major groups. There are primary brain tumors and secondary, or metastatic, brain tumors. In the latter group tumors arise or seed from different sites in the body, like the breast or the lung. The former group, the primary brain tumors, will be the focus of our show today. These are cancers that arise from cells that are resident to the brain, such as the nerve cells themselves or supporting cells called glial cells.

Chu I gather that the type of primary brain tumor is a little bit different for adults then for children.

Baehring That is correct. The spectrum of disease is age-dependent. In the adult patient population the most common tumors are those that arise from the supporting cells called gliomas. The best known one

of those is glioblastoma multiforme. In children tumors that are called embryonal tumors such as, medulloblastoma or neuroblastoma, are more common.

Chu Perhaps you can give our listeners some idea of how many patients are diagnosed each year in the United States with this primary form of brain tumor called glioblastoma.

Baehring Overall brain tumors, compared to other types of cancer, are still rare. There are only about 18,000 to 20,000 cases of newly diagnosed primary brain cancers in the United States. Glioblastoma multiforme, which is unfortunately the largest single group of brain tumors within those 20,000 cases, is the most malignant form. I would estimate that there are about 7,000 cases of it a year in the US.

Chu At what age does this kind of cancer typically present?

Baehring As for most forms of cancer, the risk of developing brain cancer is age-dependent. The age group that is most affected however, are patients older than 50 or 60 years of age, but there are exceptions and there are a substantial number of younger patients who may be affected.

Chu Any difference between men and women in terms of who can get this type of cancer?

Baehring For most subtypes, including glioblastoma, the gender distribution is fairly even, however, for some there is a slight male predominance.

Chu What are some of the main risk factors for developing brain cancer?

Baehring That is still unknown. The only established risk factor for primary brain cancer is exposure to high doses of radiation. Patients who had to have radiation for some form of brain tumor in their childhood are at a higher risk of developing a second type of brain cancer later in life. Very few cases, and that is in the order of less than 1% of all patients diagnosed with brain cancer, have a genetic predisposition of developing such. It is likely that there are other environmental factors, but research has been hampered by the fact that these tumors are rare and connections are difficult to establish.

Chu This may be a myth, but is there any association between exposure to power lines that we see in neighborhoods, and the development of brain cancer?

Baehring That has been frequently suspected whenever a cluster of brain cancer arises. An environmental cause is usually sought, and power lines have been suspected in the past, but I am not aware of any study that formally proved that exposure to electromagnetic waves played a role in one of those clusters of brain cancer.

- Chu And how about exposure to cell phones?
- Baehring There are several studies, and naturally all of them are retrospective, that found no correlation between cell phone use and the development of brain cancer. However, more recently a study was published that did seem to suggest that there may be a correlation. The risk seems to be rather low, otherwise we probably would know by now from these large-scale studies. However, as we have learned with many other environmental exposures, it may take 20 to 30 years of exposure to statistically see an increase in the incidence. So it is still an issue that requires research.
- Chu You did mention that there may be some genetic linkage, is that right?
- Baehring That is correct. There are few cases of family syndromes, and most of these syndromes have to do with the repair of errors that occur during the process of DNA replication. DNA is the molecule that contains the genetic information of the cell, and it is quite a task for the cell to duplicate this molecule prior to cell division. Many of these syndromes affect the repair process and the intricate mechanisms that monitor the accuracy of this process.
- Chu What are some of the symptoms that individuals might present with a brain tumor?
- Baehring The most common symptoms of brain cancer are actually headache and seizure. Now obviously not everybody who has a headache has to be worried that they might have brain cancer. Headache is the most common complaint that patients come to the emergency room with. However, it is headaches that get more intense week after week, month after month, a headache that is fairly localized, that should get the patient's attention. They should seek advice from their family doctor. Many times an imaging study can be performed which can result either in a diagnosis of a brain tumor, or it rules it out. Seizures are obviously more dramatic. Not every patient who has a seizure turns out to have a brain tumor. There are many causes of seizure disorders and many times no specific cause is found, but seizure would certainly warrant a workup for the possibility of a brain tumor.
- Chu Any other symptoms that one needs to be aware of?
- Baehring Sometimes symptoms are much less dramatic and insidious. Sometimes patients come who complain of memory loss or they are brought in by family members who are afraid that their loved one has come down with Alzheimer disease, so sometimes it takes on the picture of degenerative disorders like dementia.
- Chu How does one go about making the diagnosis of brain cancer?

- Baehring Once it is clinically suspected, the most sensitive test that is noninvasive is magnetic resonance imaging or MRI. Having that technique at hand has made the diagnosis of a brain tumor fairly straightforward.
- Chu If someone is claustrophobic, which I have to say yours truly is, are there alternatives to MRI?
- Baehring Well, there are technical advances in the MRI technique and now there are machines available with large bores where patients do not feel claustrophobic. We call those open MRIs. There are now even MRIs available where patients can sit or even stand or watch TV. Also scans can be done under sedation, so that is usually not a problem.
- Chu We would like to remind you to e-mail your questions to Healthline@Yale.edu or call 1-888-234-4-YCC. At this time we are going to take a short break for a Medical Minute. Please stay tuned to learn more information about the treatment of brain tumors with our special guest Dr. Baehring.

Medical Minute

This is a Medical Minute brought to you as a public service by the Yale Cancer Center. Cancer patients become cancer survivors the first day they are diagnosed. There are over 10 million cancer survivors in the US and the numbers keep growing. However, there are long-term side effects of cancer including heart problems, osteoporosis, fertility issues, impaired growth, and an increased risk of second cancers. Ending cancer treatment can be both exciting and scary. Most people are relieved to be finished with the demands of treatment but many also feel concerned about whether the cancer will come back and what they can do to prevent a relapse. Cancer survivors require long-term specialized care and support. For more information, log on to www.yalecancercenter.org.

- Chu Welcome back to Healthline. This is Dr. Ed Chu and I am in the WTIC studios with our guest Dr. Joachim Baehring, an expert in brain cancer at the Yale Cancer Center. Joachim, before the break we were talking about how to diagnose patients with brain cancer using imaging techniques, so once an MRI has been done, which is kind of the gold standard for visualizing a brain, how does one go about making the actual diagnosis?
- Baehring The actual diagnosis is dependent on a piece of tissue that one has to examine under the microscope. Rarely do we rely on the MRI alone. The first step in diagnosing a brain tumor is a surgical procedure that can either consist of a biopsy, where a small piece of tissue is retrieved from the tumor, or where the diagnostic and the first therapeutic step are combined, so that the tumor is actually resected in part or as a whole. Through this process a diagnosis is established with the first step of the treatment.
- Chu That would depend on what size the tumor appeared to be on the MRI.

- Baehring It depends on the size of the tumor. It depends on the location of the tumor. If the tumor is in a very sensitive area of the brain, such as the strength control or language control area, many times the surgical procedure has to be limited to a biopsy, since resection of the whole mass would lead to an irrecoverable neurological deficit. Location and size of the tumor, also the suspected type of tumor, are important in making a decision.
- Chu Obviously it is difficult to generalize because there are many different kinds of brain cancer, but if we deal with the most common form, the glioblastoma multiforme, what are the usual treatment options that are available to patients?
- Baehring The first step of treatment is surgery. It is well established that in most patients an attempt will be made to remove at least a large portion of the tumor, if not everything that is visible on an MRI scan. That relieves symptoms, and sometimes symptoms are only caused by the mere mass effect of the tumor, and once the pressure is relieved, patients re-acquire normal function. Intractable headaches can be resolved after surgery. Seizures are much easier to control once the tumor has been removed. For glioblastoma multiforme surgical resection is the mainstay of initial therapy.
- Chu What is the role of radiation therapy?
- Baehring Most brain tumors, first and foremost glioblastoma multiforme, require a multidisciplinary approach. The first adjuvant treatment, meaning a treatment that is provided after surgery, proven to be of benefit to this patient population was radiotherapy. The purpose of radiotherapy is to target the infiltrative edge of the tumor. These tumors are not sharply circumscribed, so even though the surgeon can take out what he can see on the MRI, there are still tumor cells left behind that are invisible on the scan and that is the target of radiotherapy. Radiotherapy actually aims at more than what was seen on the initial MRI scan.
- Chu Is there any role for chemotherapy once the tumor has been removed by surgery?
- Baehring For a large number of brain tumors, including glioblastoma multiforme, chemotherapy has been shown to further increase survival. The largest group of medications that are used for brain cancer are called alkylating agents. They are given either concomitantly with radiation, or both during radiation and after radiation. They are usually also considered adjuvant therapies. There are few indications to use chemotherapy upfront, before tumor resection is attempted.
- Chu One of the things you mentioned just a little while ago is the multidisciplinary approach, and one important point to emphasize to our listeners is that if one has a brain tumor it really is important to go to a center that approaches patients in this multidisciplinary fashion. Maybe you can explain a little bit about what is available here at the Yale Cancer Center.

- Baehring As I mentioned initially brain tumors are a rare tumor, and that means unless you are in a center that specializes in treatment of these rare cancers, doctors don't have the same exposure as we have at Yale. Now what multidisciplinary means is a combined effort between a number of departments, that is, neurosurgery, neurology, medical oncology, neuropathology, therapeutic radiology, and diagnostic radiology. In every single one of these fields you will have an expert at Yale who is not only familiar with most of the new treatment approaches, but also has one foot in the laboratory and is up to date in basic science research in brain tumors and is involved in the process of getting these new insights translated into new treatment strategies.
- Chu As part of the Yale Cancer Center we have the Yale Brain Tumor Center. How can a patient access help and information from your brain center?
- Baehring There are a couple of options. We have a website for the Yale Cancer Center with a subsite for the Brain Tumor Center. You can get directly to that at the address, yalebraintumorcenter.org. We also have a clinical coordinator who receives phone calls and then triages patients to whatever subspecialist within the center they should be initially referred to. Her name is Betsy D'Andrea, and her number is 203-737-1671.
- Chu: That's very helpful information to our listeners out there. One thing that has been discussed quite a bit these days is the use of Gamma Knife. I was wondering if you could explain to our listeners what that's all about.
- Baehring Gamma Knife radiosurgery is a very interesting new development in radiotherapy of tumors within the brain. The advantage of Gamma Knife radiosurgery is that in a single session a large dose of radiation can be given to a very small, defined area within the brain, as opposed to standard radiotherapy where not only the tumor is exposed, but also a large portion of normal brain. There are long-term side effects from exposure of normal brain to radiation. You do not have to worry as much with focused radiotherapy, or Gamma Knife radiotherapy. However, the application is limited to certain types of tumors. It is a very interesting tool for metastatic tumors but for neoblastoma it is certainly not the first treatment of choice.
- Chu We would like to remind you to e-mail your questions to Healthline@Yale.edu or call 1-888-234-4-YCC. At this point, we are going to take a short break to listen to a survivor story. Please stay tuned to learn more information about the new treatment strategies for brain cancers with our special guest Dr. Joachim Baehring.

Survivor Story

A few years ago the diagnosis of cancer was a death sentence for many patients, but today, thanks to advances in clinical research we are turning the corner in the battle against cancer. There are over 10 million cancer survivors now living in the US. They are the true heroes in the war against cancer. Here is a story of a hero from Hamden.

Ten years ago, when I was diagnosed with aplastic anemia, there was no cure. After teaching math for 35 years, I was forced to retire. Dr. Tom Duffy at the Yale Cancer Center told me about a new procedure called a mini-stem cell transplant. He encouraged me to put my life in the hands of Dr. Stuart Seropian, one of the few doctors in the county doing this procedure. On January 17, 2004, I had a stem cell transplant at the Yale Cancer Center. At age 70, I feel like a new man. I owe a great debt of gratitude to my anonymous stem cell donor and to the terrific staff at the Yale Cancer Center. They literally saved my life.

This survivor story has been brought to you by Yale Cancer Center.

- Chu Welcome back to Healthline. This is Dr. Ed Chu, and I am in the WTIC Studios with our guest Dr. Joachim Baehring, an expert in the treatment of brain cancers here at the Yale Cancer Center. Joachim, before the break, we were talking about the different treatment options that are available to patients with brain cancer. You and Dr. Piepmeier have been very actively involved in developing Convection-Enhanced Delivery Chemotherapy. Could you explain to our listeners what that is?
- Baehring Sure, I would be happy to. One thing I should explain beforehand is that one of the problems with treating brain cancer is the fact that the brain is very well protected physiologically from environmental toxins. This mechanism is called the blood-brain barrier, and it not only makes it hard for toxins to get into the brain, but also treatments that are delivered into a vein. One approach to circumvent this physiological barrier is to administer drugs directly into the brain. Convection-Enhanced Delivery is the most promising technique to achieve that goal. What it means is that at the time of tumor resection, microcatheters, usually 3 or 4, are placed around the resection cavity, the hole that's left behind by the surgeon, and then once the wound is closed these microcatheters are attached to microinfusion pumps that deliver either conventional chemotherapy drugs or newly developed drugs directly into the brain. Usually, these infusions are done in the intensive care unit and they last up to 4 days.
- Chu So the beauty of this approach is that you are directly administering the active chemotherapy agent, and hopefully it will be attacking the residual brain tumor cells and protecting the rest of the body from any side effects.

Baehring That is correct. Most of these treatments have minimal, if any, side effects in the whole system and the concentration of the drug, that can be achieved within brain tissue, is likely much higher than it is with the drug that is administered into a vein.

Chu And you were involved with the clinical study here at the Yale Cancer Center?

Baehring We were involved at various stages of the clinical study that used genetically engineered protein for brain tumor therapy. This protein contained a bacterial toxin, which is the actual mechanism by which tumor cells are intended to be killed by this molecule. It was delivered through Convection-Enhanced Delivery, and we were involved from the very early stages of this technique and also participated in what you call a Phase 3 clinical study, which is a study where the new treatment approaches are compared to standard of care.

Chu Was there much in the way of systemic side effects seen with this therapy?

Baehring We did not see any systemic side effects. Very few patients had a seizure or temporary worsening of the neurological symptoms. However, that is something that can occur spontaneously in any patient after brain surgery. So, we have to wait for the final report after the data are processed, which is not out yet.

Chu As you said, because of this blood-brain barrier, it's been very difficult for the traditional chemotherapy drugs to get into the brain and attack the brain cancer cells. What are some of the newer treatment strategies that are being taken to fight brain cancer?

Baehring There are numerous new treatment strategies. There are drugs being developed that cross this blood-brain barrier more easily. Probably the field of greatest interest in cancer in general, and brain cancer in particular, are molecules designed to target certain growth promoting pathways within brain cancer cells. This group of medication is known as small molecule inhibitors, and as the name says their molecular weight is quite small and these drugs penetrate into the brain much easier than some of the traditional compounds.

Chu Our own group in medical oncology is trying to develop a number of these novel small molecules that either target the growth factor signaling pathways, or a process that is known as angiogenesis, which is a process that inhibits the growth of new blood vessels. I am wondering if this might be a good opportunity for patients with brain cancer to be tested with some of these newer agents?

Baehring There are a number of very interesting studies going on for systemic cancer at the Yale Cancer Center, and we are in the process of establishing protocols in which brain cancer patients can be included. Some of these protocols do not include brain cancer patients for various reasons and that will be the next step, but there are certainly a lot of things going on that we are very interested in, particularly the angiogenesis inhibitors. These are drugs that prevent or interfere with the growth

of blood vessels and tumors. Tumors are dependent on this blood vessel growth because they need oxygen, otherwise they can't grow. There is some very encouraging data out there for the use of some of these angiogenesis inhibitors combined with other drugs in brain cancer and we are exploring those.

Chu Are there any trials that you would like to highlight that are presently ongoing or being offered to patients here at the Yale Cancer Center?

Baehring We have just finished accrual for a number of clinical studies. A study that will open very shortly is a study of a chemotherapy compound that is considered standard of care at this point for glioblastoma multiforme. However, we will use a higher dose than what would be considered standard of care. This is a very well tolerated treatment so it only makes sense to try to increase the dose and push it more to see what is tolerated and see if it is more effective than the standard dose. We have a trial that is going through the internal approval process for patients with a tumor called primary central nervous system lymphoma, and we are working on opening a study using one of these angiogenesis inhibitors for glioblastoma multiforme.

Chu If a patient, or a patient's family member, is interested in accessing information regarding the types of clinical trials that are available to them here at the Yale Cancer Center how do they go about doing that?

Baehring The Yale Cancer Center website, which I mentioned before, is probably the most up to date and easily accessible resource. There is a section for clinical trials where the Brain Tumor Center can be accessed. Patients or physicians can immediately see what clinical studies are currently open. Be sure to call our Clinical Coordinator, Betsy D'Andrea, to make sure all the updates are correct.

Chu And again that number is?

Baehring It is 203-737-1671.

Chu If you have questions for Dr. Baehring, or for Healthline, we encourage you to go to our website www.yalecancercenter.org for more information about cancer and the resources available to you. Before we sign off, Joachim, what are some of the key messages you would like to share with our listeners about the treatment of brain cancers?

Baehring I think the key message is that we can now look more optimistically on the treatment of brain cancer these days. I think there are a lot of very interesting new treatment approaches in the pipeline that will hopefully become available for a broader range of patients that will make a big difference in the outcome of these devastating tumors. Also, I think it is important to point out that since these tumors are so rare, patients are best treated in large referral centers where a multidisciplinary team of experts work together.

Chu Joachim, I would like to thank you for joining us today on Healthline, and remember to tune into WTIC NewsTalk 1080 every Sunday morning at 8:30 a.m. for Healthline with the Yale Cancer Center. Our next program will feature Commissioner J. Robert Galvin from the Connecticut Department of Public Health. Until then this is Dr. Ed Chu from the Yale Cancer Center wishing you a safe and healthy week.