

Chapter 1 : Metastasis: Diagnosing & Treating Metastatic Cancer | CTCA

In metastasis, cancer cells break away from where they first formed (primary cancer), travel through the blood or lymph system, and form new tumors (metastatic tumors) in other parts of the body.

Some patients, however, do not show any symptoms. Pathophysiology[edit] Metastatic tumors are very common in the late stages of cancer. The spread of metastasis may occur via the blood or the lymphatics or through both routes. The most common places for the metastases to occur are the lungs , liver , brain , and the bones. To do so, malignant cells break away from the primary tumor and attach to and degrade proteins that make up the surrounding extracellular matrix ECM , which separates the tumor from adjoining tissues. By degrading these proteins, cancer cells are able to breach the ECM and escape. The location of the metastases is not always random, with different types of cancer tending to spread to particular organs and tissues at a rate that is higher than expected by statistical chance alone. This specificity seems to be mediated by soluble signal molecules such as chemokines [12] and transforming growth factor beta. Cancer cells often opportunistically switch between different kinds of motion. Some cancer researchers hope to find treatments that can stop or at least slow down the spread of cancer by somehow blocking some necessary step in one or more kinds of motion. In particular, endothelial progenitor cells have been shown to have a strong influence on the growth of tumor blood-vessels. Endothelial progenitor cells are also critical for metastasis and angiogenesis. This novel finding meant that investigators gained the ability to track endothelial progenitor cells from the bone marrow to the blood to the tumor-stroma and even incorporated in tumor vasculature. Endothelial progenitor cells incorporated in tumor vasculature suggests that this cell type in blood-vessel development is important in a tumor setting and metastasis. Furthermore, ablation of the endothelial progenitor cells in the bone marrow can lead to a significant decrease in tumor growth and vasculature development. Therefore, endothelial progenitor cells are important in tumor biology and present novel therapeutic targets. Metastases display alterations in histone modifications, such as H3K4-methylation and H3K9-methylation, when compared to matching primary tumors. PKC- ζ inhibition or knockdown resulted an increase E-cadherin and RhoA levels while decreasing total Vimentin, phosphorylated Vimentin S39 and Par6 in metastatic melanoma cells. Primary cancers are denoted by "

Transcoelomic[edit] The spread of a malignancy into body cavities can occur via penetrating the surface of the peritoneal , pleural , pericardial, or subarachnoid spaces. For example, ovarian tumors can spread transperitoneally to the surface of the liver. Lymphatic spread[edit] Lymphatic spread allows the transport of tumor cells to regional lymph nodes near the primary tumor and ultimately, to other parts of the body. This is called nodal involvement, positive nodes, or regional disease. It is common medical practice to test by biopsy at least one lymph node near a tumor site when carrying out surgery to examine or remove a tumor. This lymph node is then called a sentinel lymph node. Lymphatic spread is the most common route of initial metastasis for carcinomas. Localized spread to regional lymph nodes near the primary tumor is not normally counted as a metastasis, although this is a sign of a worse outcome. The lymphatic system does eventually drain from the thoracic duct and right lymphatic duct into the systemic venous system at the venous angle and into the brachiocephalic veins , and therefore these metastatic cells can also eventually spread through the haematogenous route. Lymph node with almost complete replacement by metastatic melanoma. The brown pigment is focal deposition of melanin Hematogenous spread[edit] This is typical route of metastasis for sarcomas, but it is also the favored route for certain types of carcinoma, such as renal cell carcinoma originating in the kidney. Because of their thinner walls, veins are more frequently invaded than are arteries, and metastasis tends to follow the pattern of venous flow. That is, hematogenous spread often follows distinct patterns depending on the location of the primary tumor. For example, colorectal cancer spreads primarily through the portal vein to the liver. Canalicular spread[edit] Some tumors, especially carcinomas may metastasize along anatomical canalicular spaces. These spaces include for example the bile ducts, the urinary system, the airways and the subarachnoid space. The process is similar to that of transcoelomic spread. However, often it remains unclear whether simultaneously diagnosed tumors of a canalicular system are one metastatic process or in fact independent tumors caused by the same agent field cancerization. Organ-specific

targets[edit] There is a propensity for certain tumors to seed in particular organs. This was first discussed as the "seed and soil" theory by Stephen Paget over a century ago, in For example, prostate cancer usually metastasizes to the bones. In a similar manner, colon cancer has a tendency to metastasize to the liver. Stomach cancer often metastasises to the ovary in women, then it is called a Krukenberg tumor. According to the "seed and soil" theory, it is difficult for cancer cells to survive outside their region of origin, so in order to metastasize they must find a location with similar characteristics. Malignant melanoma spreads to the brain, presumably because neural tissue and melanocytes arise from the same cell line in the embryo. In these cases, doctors refer to the primary tumor as "unknown" or "occult," and the patient is said to have cancer of unknown primary origin CUP or unknown primary tumors UPT. The use of immunohistochemistry has permitted pathologists to give an identity to many of these metastases. However, imaging of the indicated area only occasionally reveals a primary. In rare cases e. It is therefore thought that some primary tumors can regress completely, but leave their metastases behind. Diagnosis[edit] The cells in a metastatic tumor resemble those in the primary tumor. Once the cancerous tissue is examined under a microscope to determine the cell type, a doctor can usually tell whether that type of cell is normally found in the part of the body from which the tissue sample was taken. For instance, breast cancer cells look the same whether they are found in the breast or have spread to another part of the body. So, if a tissue sample taken from a tumor in the lung contains cells that look like breast cells, the doctor determines that the lung tumor is a secondary tumor. Still, the determination of the primary tumor can often be very difficult, and the pathologist may have to use several adjuvant techniques, such as immunohistochemistry , FISH fluorescent in situ hybridization , and others. Despite the use of techniques, in some cases the primary tumor remains unidentified. Metastatic cancers may be found at the same time as the primary tumor, or months or years later. When a second tumor is found in a patient that has been treated for cancer in the past, it is more often a metastasis than another primary tumor. It was previously thought that most cancer cells have a low metastatic potential and that there are rare cells that develop the ability to metastasize through the development of somatic mutations. Traditional means of diagnosing cancer e. Rather, it seems that the genetic state of the primary tumor reflects the ability of that cancer to metastasize. Additionally, the metastatic-associated expression of these genes was also observed in some primary tumors, indicating that cells with the potential to metastasize could be identified concurrently with diagnosis of the primary tumor. Expression of this metastatic signature has been correlated with a poor prognosis and has been shown to be consistent in several types of cancer. Prognosis was shown to be worse for individuals whose primary tumors expressed the metastatic signature. Metastases of breast cancer , medulloblastoma and prostate cancer all had similar expression patterns of these metastasis-associated genes. Additionally, identifying the genes whose expression is changed in metastasis offers potential targets to inhibit metastasis.

Chapter 2 : Metastatic Breast Cancer - National Breast Cancer Foundation

Metastasis is a pathogenic agent's spread from an initial or primary site to a different or secondary site within the host's body; it is typically spoken of as such spread by a cancerous tumor.

Metastatic breast cancer is also classified as Stage 4 breast cancer. The cancer has spread to other parts of the body. This usually includes the lungs, liver, bones or brain. How does cancer spread, or metastasize? The spread of cancer usually happens through one or more of the following steps: Cancer cells invade nearby healthy cells. When the healthy cell is taken over, it too can replicate more abnormal cells. Cancer cells penetrate into the circulatory or lymph system. Cancer cells travel through the walls of nearby lymph vessels or blood vessels. Cancer cells are carried by the lymph system and the bloodstream to other parts of the body. Cancer cells lodge in capillaries. Cancer cells stop moving as they are lodged in capillaries at a distant location and divide and migrate into the surrounding tissue. New small tumors grow. Cancer cells form small tumors at the new location called micrometastases. There is no other option. She was diagnosed with metastatic breast cancer on April 27, Renee lived each day with hope until her passing on January 25, What are the symptoms of metastatic breast cancer? The symptoms may vary, depending on how far your breast cancer has spread and what type of tissue the new cancer growth has invaded. All symptoms should be reported to your physician. Symptoms of metastasis may vary depending on where the cancer has spread to. Here are some symptoms that vary by locations commonly associated with breast cancer metastasis. Metastasis in the bone may cause: Severe, progressive pain Bones that are more easily fractured or broken Metastasis to the brain may cause: Persistent, progressively worsening headache or pressure to the head Vision disturbances.

Chapter 3 : Advanced Cancer, Metastatic Cancer, and Bone Metastasis

Metastasis is the medical term for cancer that spreads to a different part of the body from where it started. When this happens, doctors say the cancer has "metastasized."

Different health care providers may not mean the exact same thing when they use the term advanced cancer. Advanced cancers can be locally advanced or metastatic. Metastatic cancers have spread from where they started to other parts of the body and are covered in the next section. But not all advanced cancers have spread to other parts of the body. For example, some cancers that start in the brain may be considered advanced because of their large size or closeness to important organs or blood vessels. In the same way, not all metastatic cancers are advanced cancers. Some cancers, such as testicular cancer, can spread to other parts of the body and still be very curable. Locally advanced cancer is used to describe cancer that has grown outside the organ it started in but has not yet spread to distant parts of the body. For example, locally advanced pancreatic cancer is often not curable. But other locally advanced cancers, such as some prostate cancers, may be cured. Some may use the term to describe metastatic cancer, while others might use it in other situations. Be sure you understand what the doctor is talking about and what it means for you. Advanced cancer can often be treated. Shrink the cancer Help relieve symptoms Help you live longer For some people, the cancer may already be advanced when they first learn they have the disease. For others, the cancer may not become advanced until years after it was first diagnosed. As advanced cancer grows, it can cause symptoms that may need to be treated to help control them. These symptoms can almost always be treated, even when the cancer itself no longer responds to treatment. What is metastatic cancer? Metastatic cancer is a cancer that has spread from the part of the body where it started the primary site to other parts of the body. When cancer cells break away from a tumor, they can travel to other parts of the body through the bloodstream or the lymph system. Lymph vessels are much like blood vessels, except they carry a clear fluid and immune system cells. This image shows some parts of the lymph system, like lymph nodes and lymph vessels, as well as organs and tissues that contain many lymphocytes immune cells. If the cells travel through the lymph system, they could end up in nearby lymph nodes small, bean-sized collections of immune cells or they could spread to other organs. More often, cancer cells that break off from the main tumor travel through the bloodstream. Once in the blood, they can go to any part of the body. Many of these cells die, but some may settle in a new area, start to grow, and form new tumors. This spread of cancer to a new part of the body is called metastasis. Cancer cells have to go through several steps to spread to new parts of the body: They have to be able to break away from the original tumor and enter the bloodstream or lymph system, which can carry them to another part of the body. They need to attach to the wall of a blood or lymph vessel and move through it into a new organ. They need to be able to grow and thrive in their new location. Going through all these steps means the cells that start new tumors may no longer be exactly the same as the ones in the tumor they started in. This might make them harder to treat. Treatment is also based on where the cancer started. Likewise, colon cancer that has spread to the liver is treated as metastatic colon cancer, not liver cancer. Sometimes the metastatic tumors have already begun to grow when the cancer is first found and diagnosed. And in some cases, a metastasis may be found before the original primary tumor is found. If this happens the cancer is called cancer of unknown primary. Why cancer cells tend to spread to certain parts of the body Where a cancer starts is linked to where it will spread. Once the cells are there, they can start to grow and form new tumors. This explains why breast cancer often spreads to underarm lymph nodes, but rarely to lymph nodes in the groin. Likewise, there are many cancers that commonly spread to the lungs. What is bone metastasis? A bone metastasis is an area of bone that contains cancer that spread there from somewhere else. Cancer can spread to any bone in the body, but metastases are most often found in bones near the center of the body. The spine is the most common site. Other common sites are the hip bone pelvis , upper leg bone femur , upper arm bone humerus , ribs, and the skull. Still, it often can be treated to shrink, stop, or slow its growth. Even if a cure is no longer possible, treating the cancer may be able to help you live longer and feel better. How does bone metastasis cause bone changes and other problems? Bone is the supporting framework of the body. Bones are made of a network of

fibrous tissue called matrix, minerals such as calcium that attach to the matrix and give the bone its strength and hardness, and 2 main kinds of bone cells are osteoblasts and osteoclasts. Knowing a little about these 2 kinds of cells can help you understand how bone metastases grow, and how some medicines work to treat bone metastases. The osteoblast is the cell that forms new bone, and the osteoclast is the cell that dissolves old bone. When these cells are both working right, new bone is always forming while old bone is dissolving. This helps keep the bones strong. Cancer cells can affect the bones by interfering with osteoblasts and osteoclasts: Often, the cancer cells make substances that turn on the osteoclasts. This leads to bone being broken down without new bone being made. This weakens the bones. The holes that develop when parts of bones dissolve are called osteolytic or lytic lesions. Lytic lesions are so weak that they can cause the bone to easily break. Sometimes, the cancer cells release substances that turn on the osteoblasts. This leads to new bone being made without breaking down the old bone broken down first. This makes areas of the bones harder, a condition called sclerosis. The areas of bone where this occurs are called osteoblastic or blastic lesions. Although these blastic areas are harder, the structure of the bone is not normal and these areas actually break more easily than normal bone. Bone metastasis can cause other problems as well: When cancer spreads to the bones of the spine, it can press on the spinal cord. This can cause nerve damage that may even lead to paralysis if not treated. As cancer cells damage the bones, calcium from the bones is released into the blood. This can lead to problems caused by high blood calcium levels hypercalcemia. Why do cancers metastasize to bones? For cancer cells to spread to other parts of the body, they have to go through many changes: They have to be able to break away from the original primary tumor and get into the bloodstream or lymph system, which can carry them to another part of the body. At some point they need to attach to the wall of a blood or lymph vessel and move through it, out into a new organ. They then need to be able to grow and thrive in their new location. Going through all these steps means the cells that start new tumors may no longer be exactly the same as the ones in the tumor where they started, but they will still be called the same name. For instance, breast cancer that spreads to the bone is called metastatic breast cancer, not bone cancer. Some cancers start in the bone, rather than spreading to the bones from somewhere else. Cancers that start in the bone are called primary bone cancers. These cancers are very different from bone metastases. Bone metastasis is much more common than primary bone cancers, especially in adults.

Chapter 4 : Malignancy: MedlinePlus Medical Encyclopedia

Metastatic lung cancer is a life-threatening condition that develops when cancer in another area of the body metastasizes, or spreads, to the lung. Cancer that develops at any primary site can.

AFP alpha-feto-protein HCG human chorionic gonadotropin There are several tumor markers that are less specific, and therefore, not used as a tool for diagnosing metastasis. Ultrasound is one way to evaluate the abdomen if a mass is suspected. It is a good tool for identifying fluid in the abdomen and it is good at distinguishing fluid-filled liver cysts from more solid, suspicious-appearing masses within the liver or the pelvis. CT scan computed tomography can be used to scan the head, neck, chest, abdomen and pelvis. When done with contrast, it is especially good at identifying masses within the lymph nodes, lungs, liver or other structures. It is most useful at evaluating the whole body for evidence of bone damage that is suspicious for cancer. If there is concern for a bone breaking, additional plain X-rays may be done to further define the extent of damage. MRI magnetic resonance imaging is a test using radio waves and magnets to create an image. MRI is best used to define potential damage to the spinal cord if there are bone metastasis in the vertebra of the back or to characterize brain metastases. PET scan positron emission tomography works to identify areas of hypermetabolic activity anywhere in the body. A radioactive substance is given to the patient and this attaches to glucose, which is attracted to cells that are hypermetabolic. When the scan is done, these areas "light up. In addition, not everything that is hypermetabolic is cancer. The results of these and other tests may not provide definitive information. The findings must be correlated with each other, the physical examination, symptoms, and in some cases biopsy. Treatment options Metastasis is primarily treated based on the original site of the cancer. For example, if a person has breast cancer and cancer spreads to the liver, it is still treated with the same drugs used for breast cancer "because the cancer cells themselves have not changed, they are just living in a new place. In some clinical situations, metastases may be treated in specific ways. Bone If the bone metastases are not causing pain or danger of breaking, they may be monitored or treated with drug therapy. If there is pain or the bone is fragile, radiation may be given to the location of the damage. Lung The treatment of lung metastases depends on the extent of the metastases as well as the primary cancer. In most cases, it will be treated in the same manner with the same drugs as the primary cancer. If the metastasis is causing fluid to form around the lung, a procedure thoracentesis may be done to remove the fluid to make breathing easier. Liver There are a variety of ways to treat liver metastases depending on the type and extent of the primary cancer as well as the number and size of the liver metastases. In many cases, liver metastases will be treated in the same manner with the same drugs as the primary cancer. In instances where there is limited disease, both primary and metastatic, there are several novel approaches including surgery and radiofrequency ablation RFA , for example. Organ transplant is generally NOT an option for metastatic disease. Cleveland Clinic is a non-profit academic medical center. Advertising on our site helps support our mission. We do not endorse non-Cleveland Clinic products or services.

Chapter 5 : Understanding Advanced Cancer, Metastatic Cancer, and Bone Metastasis

The term "cancer of unknown primary" refers to a condition in which a patient has metastatic malignancy without an identified primary source. This is a very heterogeneous disease in which the type of tumour, the extent of spread, and the outcome of treatment all vary widely.

In some instances, this predictability can guide doctors and help keep an eye on certain parts of the body that are susceptible to tumors. Because mesothelioma is not generally diagnosed until its later stages usually stage 3 or 4, metastatic disease is common at the time of diagnosis. Mesothelioma metastasis, however, can also occur as the disease continues to progress. How Quickly Does Mesothelioma Metastasize? Mesothelioma is known as a particularly aggressive cancer with a range of development rates. What makes it so aggressive, and how does this affect life expectancy? It almost always develops in the chest cavity or the abdominal cavity, where it readily affects vital organs like the lungs and heart. Tumor Types Certain types of tumor cells are also particularly dangerous and can spread more efficiently. These factors can lead to short survival times of a year or less, but proper treatment can help prolong life. Unlike many other cancers, mesothelioma rarely spreads to the bones or brain, but normally affects the organs around the lungs on the side of the body in which the original tumor was found. This is because the disease is most often located in or near the lungs, which transfer oxygen throughout the body. Therefore, cancer cells may be able to enter the bloodstream and circulate through the body. Cancer progression can sometimes be detected through diagnostic imaging tests, which include MRIs or CT scans. Doctors usually suspect that a cancer has spread when a patient complains of symptoms that are not generally associated with asbestos cancer. At that time, tests or biopsies will be performed. How Does Mesothelioma Spread? Mesothelioma can spread throughout the body in a number of ways. Metastasis generally occurs when cancer cells travel through the bloodstream or lymphatic system to distant sites. Once mesothelioma cells have spread around the body, they can invade any nearby organs and cause secondary tumors to develop. Cancer also can grow and spread through angiogenesis, a process that forms new blood vessels in the body. This happens when cancerous cells release molecules that reach nearby healthy tissue and form new blood vessels. The fresh supply of oxygen and nutrients from these blood vessels allows cancer cells to develop into secondary tumors. Researchers are studying ways to promote and block angiogenesis to develop a number of anti-angiogenic medications. These treatments may be the key to slowing or halting the spread of cancer. Drugs being evaluated for mesothelioma metastasis include semaxanib SU, thalidomide and tetrathiomolybdate. In clinical trials, the three medications demonstrate an ability to help stabilize the disease and increase survival. Get a Free Mesothelioma Guide Free information, books, wristbands and more for patients and caregivers. Stages of Cancer Development Patients diagnosed at stage I have the best prognosis, living a median of two to three years. Doctors use a mesothelioma staging system to help gauge the development of pleural cancer. The disease is the least developed during the early stages, when the cancer is localized in or around its origin site. At these stages, the cancer may be treated with a combination of potentially curative measures such as surgery, chemotherapy and radiation therapy. Patients diagnosed at stage 1 have the best prognosis, living a median of two to three years. By stage 4, the cancer has metastasized, and tumors have developed in distant areas of the body. This is the most difficult to treat because the cancer is so widespread. At this stage of development, treatment is limited to palliative, symptom-controlling care. This leads to a life expectancy of less than a year. Pleural Metastases For many years, doctors considered pleural mesothelioma a localized disease with limited ability to metastasize to other parts of the body. However, a postmortem study revealed the majority of the mesothelioma patients involved experienced cancer spread to the opposite side of the chest and distant sites. A similar review of people who died of pleural mesothelioma found that the most common sites for mesothelioma metastasis include: By stage 3 and 4, pleural mesothelioma metastasizes through the blood to distant sites in more than 10 percent of cases. By the time most people receive a mesothelioma diagnosis, their cancer is already in the later stages of development. If the cancer has spread to distant parts of the body, treatment options tend to be palliative in nature, meaning they aim to relieve symptoms and provide comfort rather than cure the disease. Peritoneal

Metastases In its early stages, peritoneal mesothelioma generally does not spread beyond the peritoneal cavity, which contains the stomach, spleen, liver, intestines and other abdominal organs. As the disease progresses, cancer cells spread through the lymph nodes and blood. This can cause secondary tumors to develop in nearby organs and distant locations. Sites where peritoneal mesothelioma tends to spread include:

Chapter 6 : Metastasis - Wikipedia

Metastatic breast cancer is also classified as Stage 4 breast cancer. The cancer has spread to other parts of the body. The cancer has spread to other parts of the body. This usually includes the lungs, liver, bones or brain.

Chapter 7 : Benign and Malignant Tumors: What is the Difference?

What is metastasis? Metastasis is a word used to describe the spread of cancer. Unlike normal cells, cancer cells have the ability to grow outside of the place in the body where they originated.

Chapter 8 : Bone metastasis - Wikipedia

Metastatic cancer: Any cancer that has spread to other parts of the body. More detailed information about the symptoms, causes, and treatments of Metastatic cancer is.

Chapter 9 : Metastatic Cancer: What Is Metastasis? | Cleveland Clinic

metastatic cancer Cancer which has spread in a non-contiguous fashionâ€”by the blood, haematogenously; by the lymphatic, trans-coelomicallyâ€”from a primary site of origin to a distant site.