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| Skin Cancer Treatment | Alternative Skin Cancer Treatment |

Home

Treatment Information Cancer Types Physician Information Prevention Information Contact us

About Us

Free Consultation

Donations Accepted

Newsletter

Site Survey

Privacy / Legal Issues

Site Map

Links

Cancer Treatment

Printer Friendly Version
Click Here



The Science Behind CAAT

Cancer Types

Bladder Cancer Treatment

Brain Cancer Treatment

Breast Cancer Treatment

Cervical Cancer Treatment

Colorectal Cancer Treatment

Esophageal Cancer Treatment

Kidney Cancer Treatment

Leukemia Cancer Treatment

• Acute Lymphocytic Leukemia Treatment

• Acute Myeloid Leukemia Treatment

• Chronic Lymphocytic Leukemia Treatment

• Chronic Myelogenous Leukemia Treatment

Liver Cancer Treatment

Lung Cancer Treatment

Lymphoma Treatment

• Hodgkins Disease Treatment

• Non-Hodgkins Disease Treatment

Ovarian Cancer Treatment

Pancreatic Cancer Treatment

Prostate Cancer Treatment

Skin Cancer Treatment

Thyroid Cancer Treatment

Skin Cancer

What is Skin Cancer?

Skin cancer is the most common of all cancers. It is the most common form of human cancer. It is estimated that over 1 million new cases occur annually. The annual rates of all forms of skin cancer are increasing each year, representing a growing public concern. It has also been estimated that nearly half of all Americans who live to age 65 will develop skin cancer at least once.

The most common warning sign of skin cancer is a change in the appearance of the skin, such as a new growth or a sore that will not heal.

There are three main types of skin cancers:

- **Squamous Cell Carcinoma**

The top layer of the epidermis is mostly made up of flat, scale-like cells called squamous cells. Approximately 16% of skin cancers begin in this layer, and are called squamous cell carcinoma. They usually arise from sun exposure, but can appear on skin that has been burned, damaged by chemicals, or exposed to x-rays.

- **Basal Cell Carcinoma**

Under squamous cells, in the lower epidermis are round cells known as basal cells. About 80% of skin cancers arise from this layer in skin that has been exposed to the sun, and are called basal cell carcinoma. Basal cell carcinomas most often form on the head and neck.

- **Melanoma**

The deepest layer of the epidermis contains scattered cells called melanocytes, which produce the melanin that gives skin color. Melanoma starts in melanocytes, and it is the most serious of the three cancer types. For more information, see the summary on melanoma.

Basal cell and squamous cell cancers are known as non-melanoma skin cancers, to distinguish them from melanoma, which is much more dangerous. Basal cell carcinoma grows slowly and seldom spreads (metastasizes) to other parts of the body. Squamous cell carcinoma also rarely spreads, but is more likely to do so than basal cell carcinoma.

As we well know, there are many kinds of cancer; unfortunately they all come about because of the out-of-control growth of abnormal cells.

Basal cell carcinoma is the most common form of skin cancer. The second most common type of skin malignancy is squamous cell carcinoma. Although these 2 types of skin cancer are the most common of all malignancies, they account for less than 0.1% of patient deaths due to cancer. Both of these types of skin cancer are more likely to occur in individuals of light complexion who have had significant exposure to sunlight, and both types of skin cancers are more common in the southern latitudes of the Northern hemisphere. The overall cure rate for both types of skin cancer is directly related to the stage of the disease and the type of treatment used. However, since neither basal cell carcinoma nor squamous cell carcinoma are reportable diseases, precise 5-year cure rates are not known. Although basal cell carcinoma and squamous cell carcinoma are by far the most frequent types of skin tumors, the skin can also be the site of a large variety of malignant neoplasms. These other types of malignant disease include malignant melanoma, cutaneous T-cell lymphomas (mycosis fungoides), Kaposi's sarcoma, extramammary Paget's disease, apocrine carcinoma of the skin, and metastatic malignancies from various primary sites.

Basal cell carcinoma

Basal cell carcinoma is at least 3 times more common than squamous cell carcinoma in non-immunocompromised patients. It usually occurs on sun-exposed areas of skin, and the nose is the most frequent site. Although there are many different clinical presentations for basal cell carcinoma, the most characteristic type is the asymptomatic nodular or nodular ulcerative lesion that is elevated from the surrounding skin and has a pearly quality and contains telangiectatic vessels. It is recognized that basal cell carcinoma has a tendency to be locally destructive. High-risk areas for tumor recurrence include the central face (periorbital region, eyelids, nasolabial fold, nose-cheek angle), postauricular region, pinna, ear canal, forehead, and scalp. A specific subtype of basal

cell carcinoma is the morphea-form type. It typically appears as a scar-like, firm plaque and because of indistinct clinical tumor margins, it is difficult to treat adequately with traditional treatments.

Squamous cell carcinoma

Squamous cell tumors also tend to occur on sun-exposed portions of the skin such as the ears, lower lip, and dorsa of the hand. However, squamous cell carcinomas that arise in areas of non-sun-exposed skin or that originate de novo on areas of sun-exposed skin are prognostically worse since they have a greater tendency to metastasize. Chronic sun damage, sites of prior burns, arsenic exposure, chronic cutaneous inflammation as seen in long standing skin ulcers, and sites of previous x-ray therapy are predisposed to the development of squamous cell carcinoma.

Actinic keratosis

Actinic keratoses are potential precursors of squamous cell carcinoma. These typical red scaly patches usually arise on areas of chronically sun-exposed skin, and are likely to be found on the face and dorsal aspects of the hand. Although the vast majority of actinic keratoses do not become squamous cell carcinomas, it is thought that as many as 5% of actinic keratoses will evolve into this locally invasive carcinoma. Due to this premalignant potential, the destruction of actinic keratoses is advocated.

Healthy Cells vs. Cancer Cells

Healthy cells are like a cat. They need structure to determine the size of bones and shape of the body, tail and whiskers. The DNA in genes and chromosomes determine this. They need energy to play and prowl and sustain life. This is derived from chemicals in food. Cats need a system to deliver chemicals (food nutrients like amino acids, carbohydrates, fats, vitamins and minerals) to all parts of their body. These are the blood vessels. Growth factors take a kitten into a lazy old cat, all the while helping it to function normally.

The body and its cells are mostly made up of protein. The building blocks of proteins are substances called amino acids that in the form of enzymes and hormones literally control every chemical reaction within the cells. When these are modified, different messages are sent to a complex control system that can alter their function. There are twenty different kinds of amino acids that are essential to life. Twelve of these can be synthesized within the body however; eight must be supplied by the daily diet.

Structure	
Normal Cells	Cancer Cells
DNA in genes and chromosomes go about their business in a normal way.	Cancer cells develop a different DNA or gene structure or acquire abnormal numbers of chromosomes.
Cells divide in an orderly way to produce more cells only when the body needs them.	Cells continue to be created without control or order. If not needed, a mass of tissue is formed which is called a tumor.
Energy	
Normal Cells	Cancer Cells
Cells derive 70% of their energy from a system called the "Krebs Cycle."	Cells have a defective "Krebs Cycle" and derive little or no energy from it.
Cells derive only 20% of their energy from a system called "Glycolosis."	Cancer cells derive almost all their energy from "Glycolosis."
Cells derive most of their energy with the use of oxygen.	Cells derive most of their energy in the absence of oxygen.
Blood Vessels	
Normal Cells	Cancer Cells
Cells have a built-in blood vessel system.	Cells do not have a built-in blood vessel system. They require more of certain amino acids to grow.

Growth Factors	
Normal Cells	Cancer Cells
While similar to cancer cells, the amount of them is more in balance to produce a more normal level of activity.	These cells have over produced, require more chemicals (food) and are over active.
Functions	
Normal Cells	Cancer Cells
The enzymes and hormones go about business in a normal balanced manner.	The enzymes and hormones are either over active or under active.
Tumors are Different	
Benign	Malignant
Benign tumors are not cancerous. They do not invade nearby tissues nor spread to other parts of the body. They can be removed and are not a threat to	Malignant tumors are cancerous. They can invade and damage nearby tissues and organs and they can break away and enter the blood stream to form new

life.

tumors in other parts of the body. The spread of cancer is called metastasis.

What is screening?

Screening is looking for cancer before a person has any symptoms. This can help find cancer at an early stage. When abnormal tissue or cancer is found early, it may be easier to treat. By the time symptoms appear, cancer may have begun to spread.

Scientists are trying to better understand which people are more likely to get certain types of cancer. They also study the things we do and the things around us to see if they cause cancer. This information helps doctors recommend who should be screened for cancer, which screening tests should be used, and how often the tests should be done.

It is important to remember that your doctor does not necessarily think you have cancer if he or she suggests a screening test. Screening tests are given when you have no cancer symptoms.

If a screening test result is abnormal, you may need to have more tests done to find out if you have cancer. These are called diagnostic tests.

Screening tests have risks.

Decisions about screening tests can be difficult. Not all screening tests are helpful and most have risks. Before having any screening test, you may want to discuss the test with your doctor. It is important to know the risks of the test and whether it has been proven to reduce the risk of dying from cancer.

The risks of melanoma screening tests include the following:

Finding melanoma may not improve health or help a person live longer.

Screening may not improve your health or help you live longer if you have advanced melanoma or if it has already spread to other places in your body.

Some cancers never cause symptoms or become life-threatening, but if found by a screening test, the cancer may be treated. It is not known if treatment of these cancers would help you live longer than if no treatment were given, and treatments for cancer may have serious side effects.

False-negative test results can occur.

Screening test results may appear to be normal even though melanoma is present. A person who receives a false-negative test result (one that shows there is no cancer when there really is) may delay seeking medical care even if there are symptoms.

False-positive test results can occur.

Screening test results may appear to be abnormal even though no cancer is present. A false-positive test result (one that shows there is cancer when there really isn't) can cause anxiety and is usually followed by more tests (such as a biopsy), which also have risks.

A biopsy may cause scarring.

When a skin biopsy is done, the doctor will try to leave the smallest scar possible, but there is a risk of scarring and infection.

Your doctor can advise you about your risk for skin cancer and your need for screening tests.

Basal Cell Carcinoma of the Skin

The traditional methods of treatment involve the use of cryosurgery, radiation therapy, electrodesiccation and curettage, and simple excision. Each of these methods is useful in specific clinical situations. Depending on case selection, these methods have cure rates ranging from 85% to 95%. Mohs micrographic surgery, a newer surgical technique, has the highest 5-year cure rates for surgical treatment of both primary (96%) and recurrent (90%) tumors. This method uses microscopic control to evaluate the extent of tumor invasion.

Standard treatment options:

1. Mohs micrographic surgery. Although this method is complicated and requires special training, it has the highest cure rate of all surgical treatments because the tumor is microscopically delineated until it is completely removed. While other treatment methods for recurrent basal cell carcinoma have failure rates of about 50%, cure rates have been reported at 96% when treated by Mohs micrographic surgery. In addition, it is indicated for the treatment of primary basal cell carcinomas when they occur at sites known to have a high initial treatment failure rate with traditional methods (periorbital area, nasolabial fold, nose-cheek angle, posterior cheek sulcus, pinna, ear canal, forehead, scalp, or tumors arising in a scar).

Mohs micrographic surgery is also indicated for tumors with poorly defined clinical borders, tumors with diameters larger than 2 cm, tumors with histopathologic features showing morpheaform or sclerotic patterns, and tumors arising in regions where maximum preservation of uninvolved tissue is desirable, such as eyelid, nose, finger, and genitalia.

2. Simple excision with frozen or permanent sectioning for margin evaluation. This traditional surgical treatment usually relies on surgical margins ranging from 3 to 10 mm, depending on the diameter of the tumor. Tumor recurrence is not uncommon because only a small fraction of the total tumor margin is examined pathologically. Recurrence rate for primary tumors greater than 1.5 cm in diameter is at least 12% within 5 years; if the primary tumor measures larger than 3 cm, the 5-year recurrence rate is 23.1%. Primary tumors of the ears, eyes, scalp, and nose have recurrence rates ranging from 12.9% to 25%.
3. Electrodesiccation and curettage. This method is the most widely employed method for removing primary basal cell carcinomas. Although it is a quick method for destroying the tumor, adequacy of treatment cannot be assessed immediately since the surgeon cannot visually detect the depth of microscopic tumor invasion.

Tumors with diameters ranging from 2 to 5 mm have a 15% recurrence rate after treatment with electrodesiccation and curettage. When tumors larger than 3 cm are treated with electrodesiccation and curettage, a 50% recurrence rate should be expected within 5 years.

4. Cryosurgery. Cryosurgery may be considered for small, clinically well defined primary tumors. It is especially useful for debilitated patients with medical conditions that preclude other types of surgery. However, the absolute contraindications for cryosurgery include patients with abnormal cold tolerance, cryoglobulinemia, cryofibrinogenemia, Raynaud's disease (only for treatment of lesions on hands and feet), and platelet deficiency disorders. Morphea or sclerosing basal cell carcinoma should not be treated by cryosurgery. Relative contraindications to cryosurgery include tumors of the scalp, ala nasi, nasolabial fold, tragus, postauricular sulcus, free eyelid margin, upper lip vermilion border, and lower legs. Caution should also be used before treating nodular ulcerative neoplasia greater than 3 cm, carcinomas fixed to the underlying bone or cartilage, tumors situated on the lateral margins of the fingers and at the ulnar fossa of the elbow, or recurrent carcinomas following surgical excision. There is significant morbidity associated with the use of cryosurgery. Edema is common following treatment, especially around the periorbital region, temple, and forehead. Treated tumors usually exude necrotic material, after which an eschar forms and persists for about 4 weeks. Permanent pigment loss at the treatment site is unavoidable. Atrophy and hypertrophic scarring have been reported, as well as instances of motor and sensory neuropathy.
5. Radiation therapy. Radiation is a logical treatment choice, particularly for primary lesions requiring difficult or extensive surgery (e.g., eyelids, nose, ears). It eliminates the need for skin grafting when surgery would result in an extensive defect. Cosmetic results are generally good to excellent with a small amount of hypopigmentation or telangiectasia in the treatment port. Radiation therapy can also be used for lesions that recur after a primary surgical approach. Radiation therapy is contraindicated for patients with xeroderma pigmentosum, epidermodysplasia verruciformis, or the basal cell nevus syndrome because it may induce more tumors in the treatment area.
6. Carbon dioxide laser. This method is most frequently applied to the superficial type of basal cell carcinoma. It may be considered when a bleeding diathesis is present, since bleeding is unusual when this laser is used.
7. Topical fluorouracil (5-FU). This method may be helpful in the management of selected patients with superficial basal cell carcinomas. Careful and prolonged follow-up is required, since deep follicular portions of the tumor may escape treatment and result in future tumor recurrence.
8. Systemic retinoids. Although several clinical trials have shown some efficacy for currently available systemic retinoids in both chemotherapy and chemoprevention, the long-term toxicity of these agents generally excludes them as treatment choices for most patients. Studies are exploring their value as cancer preventive agents in patients at high risk for developing multiple tumors.
9. Interferon alfa. Several early studies have shown variable responses of basal cell carcinoma to intralesional interferon alfa. Further reports are awaited until this treatment may be recommended for routine clinical practice.
10. Photodynamic therapy. Photodynamic therapy with photosensitizers may be effective treatment for superficial epithelial skin tumors.

Follow-up:

- Following treatment for basal cell carcinoma, the patient should be clinically examined every 6 months for 5 years. Thereafter, the patient should be examined for recurrent tumor or new primary tumors at yearly intervals. It has been prospectively found that 36% of patients who develop a basal cell carcinoma will develop a second primary basal cell carcinoma within the next 5 years. Early diagnosis and treatment of

recurrent basal cell carcinomas or another primary basal cell carcinoma is desirable since the treatment of the disease in its earliest stages results in less patient morbidity.

Squamous Cell Carcinoma of the Skin

Localized squamous cell carcinoma of the skin is a highly curable disease. The traditional methods of treatment involve the use of cryosurgery, radiation therapy, electrodesiccation and curettage, and simple excision. Each of these methods may be useful in specific clinical situations. Of all treatment methods available, Mohs micrographic surgery has the highest 5-year cure rate for both primary and recurrent tumors. This method uses microscopic control to evaluate the extent of tumor invasion. Lymphadenectomy is indicated when regional lymph nodes are involved.

Standard treatment options:

1. Mohs micrographic surgery. Although this method is complicated and requires special training, it has the highest cure rate of all surgical treatments because the tumor is microscopically delineated until it is completely removed. It is indicated for the treatment of primary squamous cell carcinomas when they occur at sites known to have a high initial treatment failure rate following traditional methods, primary tumors with poorly defined clinical borders, primary tumors with diameters larger than 2 cm, or primary tumors arising in regions where the maximum preservation of uninvolved tissue is desirable, such as the face, head, and genitalia. It should be used for squamous cell carcinomas that show perineural invasion since tumor transit along nerves may extend many centimeters away from the primary or recurrent tumor site. Recurrent squamous cell carcinomas can also be treated with this technique.
2. Simple excision with frozen or permanent sectioning for margin evaluation. This traditional surgical treatment usually relies on surgical margins ranging from 3 to 10 mm, depending on the diameter of the original tumor. Tumor recurrence is not uncommon because only a small fraction of the total tumor margin is examined pathologically.
3. Electrodesiccation and curettage. This is a quick method for destroying the tumor, but the adequacy of treatment cannot be assessed immediately since the surgeon cannot visually detect the depth of microscopic tumor invasion. It should be reserved for very small primary tumors since this disease has metastatic potential.
4. Cryosurgery. Cryosurgery is used for clinically well defined in situ tumors. It is especially useful for debilitated patients with medical conditions that preclude other types of surgery. However, the absolute contraindications for cryosurgery include patients with abnormal cold tolerance, cryoglobulinemia, cryofibrinogenemia, Raynaud's disease, and platelet deficiency disorders. Relative contraindications to cryosurgery include tumors of the scalp, ala nasi, nasolabial fold, tragus, postauricular sulcus, free eyelid margin, upper lip vermilion border, and lower legs. Caution should also be used before treating nodular ulcerative neoplasia greater than 3 cm, carcinomas fixed to the underlying bone or cartilage, tumors situated on the lateral margins of the fingers and at the ulnar fossa of the elbow, or recurrent carcinomas following surgical excision. There is significant morbidity associated with the use of cryosurgery. Edema is common following treatment, especially around the periorbital region, temple, and forehead. Treated tumors usually exude necrotic material, after which an eschar forms and persists for about 4 weeks. Permanent pigment loss at the treatment site is unavoidable. Atrophy and hypertrophic scarring have been reported, as well as instances of motor and sensory neuropathy.
5. Radiation therapy. Radiation is a logical treatment choice, particularly for primary lesions requiring difficult or extensive surgery (e.g., eyelids, nose, ears). It eliminates the need for skin grafting when surgery would result in an extensive defect. Cosmetic results are generally good to excellent with a small amount of hypopigmentation or telangiectasia in the treatment port. Radiation therapy can also be utilized for lesions that recur after a primary surgical approach. Radiation therapy is contraindicated for patients with xeroderma pigmentosum, epidermodysplasia verruciformis, or the basal cell nevus syndrome because it may induce more tumors in the treatment area.
6. Topical fluorouracil (5-FU). This method may be helpful in the management of selected in situ squamous cell carcinomas (Bowen's disease). Careful and prolonged follow-up is required since deep follicular portions of the tumor may escape treatment and result in future tumor recurrence.
7. Carbon dioxide laser. This method may be helpful in the management of selected squamous cell carcinoma in situ. It may be considered when a bleeding diathesis is present, since bleeding is unusual when this laser is used.
8. Interferon alfa. Clinical trials are ongoing to treat squamous cell carcinoma with intralesional interferon alfa. The results should be available in several years. One report shows the combination of interferon alfa and retinoids is effective treatment for squamous cell carcinoma.

Follow-up:

- Since squamous cell carcinomas have definite metastatic potential, these patients should be re-examined every 3 months for the first several years and then followed indefinitely at 6-month intervals.

Actinic Keratosis

Actinic keratosis commonly appears in regions of chronic sun exposure such as the face and dorsa of the hands. Actinic cheilitis is a related condition that usually appears on the lower lips. They represent early epithelial transformation that may eventually evolve into invasive squamous cell carcinoma. Actinic keratosis is a premalignant condition that should be treated with one of the methods available.

Standard treatment options:

1. Topical agents:
 1. Trichloroacetic acid.
 2. Phenol.
 3. Fluorouracil (5-FU): Treats the clinically obvious disease as well as regions of subclinical involvement. It is usually associated with a superior cosmetic result.
 4. Retinoic acid: Being evaluated for treatment and prevention of actinic keratosis.
2. Cryosurgery.
3. Electrodesiccation and curettage.
4. Dermabrasion.
5. Shave excision.
6. Carbon dioxide laser.

Melanoma is a disease in which malignant (cancer) cells form in the skin cells called melanocytes (cells that color the skin).

Melanocytes are found throughout the lower part of the epidermis. They produce melanin, the pigment that gives skin its natural color. When skin is exposed to the sun, melanocytes produce more pigment, causing the skin to tan, or darken.

The skin is the body's largest organ. It protects against heat, sunlight, injury, and infection. The skin has 2 main layers: the epidermis (upper or outer layer) and the dermis (lower or inner layer).

When melanoma starts in the skin, the disease is called cutaneous melanoma. This PDQ summary is about cutaneous (skin) melanoma. Melanoma may also occur in the eye and is called intraocular or ocular melanoma. (Refer to the PDQ summary on Intraocular (Eye) melanoma Treatment for more information.)

Melanoma is more aggressive than basal cell skin cancer or squamous cell skin cancer. (Refer to the PDQ summary on Skin cancer Treatment for more information on basal cell and squamous cell skin cancer.)

Melanoma can occur anywhere on the body.

In men, melanoma is often found on the trunk (the area from the shoulders to the hips) or the head and neck. In women, melanoma often develops on the arms and legs. Melanoma usually occurs in adults, but it is sometimes found in children and adolescents.

Unusual moles, exposure to sunlight, and health history can affect the risk of developing melanoma.

Risk factors include the following:

- Unusual moles.
- Exposure to natural sunlight.
- Exposure to artificial ultraviolet light (tanning booth).
- Family or personal history of melanoma.
- Being white and older than 20 years.
- Red or blond hair.
- White or light-colored skin and freckles.
- Blue eyes.

Possible signs of melanoma include a change in the appearance of a mole or pigmented area.

These and other symptoms may be caused by melanoma or by other conditions. A doctor should be consulted if any of the following problems occur:

- A mole that:
 - changes in size, shape, or color.
 - has irregular edges or borders.
 - is more than 1 color.
 - is asymmetrical (if the mole is divided in half, the 2 halves are different in size or shape).
 - itches.
 - oozes, bleeds, or is ulcerated (a hole forms in the skin when the top layer of cells breaks down and the underlying tissue shows through).
- Change in pigmented (colored) skin.
- Satellite moles (new moles that grow near an existing mole).

Tests that examine the skin are used to detect (find) and diagnose melanoma.

If a mole or pigmented area of the skin changes or looks abnormal, the following tests and procedures can help detect and diagnose melanoma:

- Skin examination: A doctor or nurse examines the skin to look for moles, birthmarks, or other pigmented areas that look abnormal in color, size, shape, or texture.
- Biopsy: A local excision is done to remove as much of the suspicious mole or lesion as possible. A pathologist then looks at the tissue under a microscope to check for cancer cells. Because melanoma can be hard to diagnose, patients should consider having their biopsy sample checked by a second pathologist.

Suspicious areas should not be shaved off or cauterized (destroyed with a hot instrument, an electrical current, or a caustic substance).

After melanoma has been diagnosed, tests are done to find out if cancer cells have spread within the skin or to other parts of the body.

The process used to find out whether cancer has spread within the skin or to other parts of the body is called staging. The information gathered from the staging process determines the stage of the disease. It is important to know the stage in order to plan treatment.

The following tests and procedures may be used in the staging process:

- Wide local excision: A surgical procedure to remove some of the normal tissue surrounding the area where melanoma was found, to check for cancer cells.
- Lymph node mapping and sentinel lymph node biopsy: Procedures in which a radioactive substance and/or blue dye is injected near the tumor. The substance or dye flows through lymph ducts to the sentinel node or nodes (the first lymph node for cancer cells). If no cancer cells are detected, it may not be necessary to remove additional nodes.
- Chest x-ray: An x-ray of the organs and bones inside the chest. An x-ray is a type of energy beam that can go through the body and onto film, making a picture of areas inside the body.
- CT scan (CAT scan): A procedure that makes a series of detailed pictures of areas inside the body, taken from different angles. The pictures are made by a computer linked to an x-ray machine. A dye may be injected into a vein or swallowed to help the organs or tissues show up more clearly. This procedure is also called computed tomography, computerized tomography, or computerized axial tomography. For melanoma, pictures may be taken of the chest, abdomen, and pelvis.
- MRI (magnetic resonance imaging): A procedure that uses a magnet, radio waves, and a computer to make a series of detailed pictures of areas inside the body. This procedure is also called nuclear magnetic resonance imaging (NMRI).
- PET scan (positron emission tomography scan): A procedure to find malignant tumor cells in the body. A small amount of radionuclide glucose (sugar) is injected into a vein. The PET scanner rotates around the body and makes a picture of where glucose is being used in the body. Malignant tumor cells show up brighter in the picture because they are more active and take up more glucose than normal cells.
- Laboratory tests: Medical procedures that test samples of tissue, blood, urine, or other substances in the

body. These tests help to diagnose disease, plan and check treatment, or monitor the disease over time.

The results of these tests are viewed together with the results of the tumor biopsy to determine the melanoma stage.

The following stages are used for melanoma:

Stage 0

In stage 0, melanoma is found only in the epidermis (outer layer of the skin). Stage 0 is also called melanoma in situ.

Stage I

Stage I is divided into stages IA and IB.

- Stage IA: In stage IA, the tumor is not more than 1 millimeter thick, with no ulceration. The tumor is in the epidermis and upper layer of the dermis.
- Stage IB: In stage IB, the tumor is either:
 - not more than 1 millimeter thick, with ulceration, and may have spread into the dermis or the tissues below the skin; or
 - 1 to 2 millimeters thick, with no ulceration.

Stage II

Stage II is divided into stages IIA, IIB, and IIC.

- Stage IIA: In stage IIA, the tumor is either:
 - 1 to 2 millimeters thick, with ulceration; or
 - 2 to 4 millimeters thick, with no ulceration.
- Stage IIB: In stage IIB, the tumor is either:
 - 2 to 4 millimeters thick, with ulceration; or
 - more than 4 millimeters thick, with no ulceration.
- Stage IIC: In stage IIC, the tumor is more than 4 millimeters thick, with ulceration.

Stage III

In stage III, the tumor may be any thickness, with or without ulceration, and:

- has spread to 1 or more lymph nodes; or
- has spread into the nearby lymph system but not into nearby lymph nodes; or
- has spread to lymph nodes that are matted (not moveable); or
- satellite tumors (additional tumor growths within 2 centimeters of the original tumor) are present and nearby lymph nodes are involved.

Stage IV

In stage IV, the tumor may be any thickness, with or without ulceration, may have spread to 1 or more nearby lymph nodes, and has spread to other places in the body.

Certain factors affect prognosis (chance of recovery) and treatment options.

The prognosis (chance of recovery) and treatment options depend on the following:

- The stage of melanoma (whether cancer is found in the outer layer of skin only, or has spread to the lymph nodes, or to other places in the body).
- Whether there was bleeding or ulceration at the primary site.
- The location and size of the tumor.
- The patient's general health.

Although many people are successfully treated, melanoma can recur (come back).

Four types of standard treatment are used:

1. Surgery

Surgery to remove the tumor is the primary treatment of all stages of melanoma. The doctor may remove the tumor using the following operations:

- Local excision: Taking out the melanoma and some of the normal tissue around it.
- Wide local excision with or without removal of lymph nodes.
- Lymphadenectomy: A surgical procedure in which the lymph nodes are removed and examined to see whether they contain cancer.
- Sentinel lymph node biopsy: The removal of the sentinel lymph node (the first lymph node the cancer is likely to spread to from the tumor) during surgery. A radioactive substance and/or blue dye is injected near the tumor. The substance or dye flows through the lymph ducts to the lymph nodes. The first lymph node to receive the substance or dye is removed for biopsy. A pathologist views the tissue under a microscope to look for cancer cells. If cancer cells are not found, it may not be necessary to remove more lymph nodes.

Skin grafting (taking skin from another part of the body to replace the skin that is removed) may be done to cover the wound caused by surgery.

Even if the doctor removes all the melanoma that can be seen at the time of the operation, some patients may be offered chemotherapy after surgery to kill any cancer cells that are left. Chemotherapy given after surgery, to increase the chances of a cure, is called adjuvant therapy.

2. Chemotherapy

Chemotherapy is a cancer treatment that uses drugs to stop the growth of cancer cells, either by killing the cells or by stopping the cells from dividing. When chemotherapy is taken by mouth or injected into a vein or muscle, the drugs enter the bloodstream and can reach cancer cells throughout the body (systemic chemotherapy). When chemotherapy is placed directly into the spinal column, an organ, or a body cavity such as the abdomen, the drugs mainly affect cancer cells in those areas (regional chemotherapy).

In treating melanoma, chemotherapy drugs may be given as a hyperthermic isolated limb perfusion. This technique sends anticancer drugs directly to the arm or leg in which the cancer is located. The flow of blood to and from the limb is temporarily stopped with a tourniquet, and a warm solution containing anticancer drugs is put directly into the blood of the limb. This allows the patient to receive a high dose of drugs in the area where the cancer occurred.

The way the chemotherapy is given depends on the type and stage of the cancer being treated.

3. Radiation therapy

Radiation therapy is a cancer treatment that uses high-energy x-rays or other types of radiation to kill cancer cells. There are two types of radiation therapy. External radiation therapy uses a machine outside the body to send radiation toward the cancer. Internal radiation therapy uses a radioactive substance sealed in needles, seeds, wires, or catheters that are placed directly into or near the cancer. The way the radiation therapy is given depends on the type and stage of the cancer being treated.

Treatment Options for Recurrent Melanoma

Treatment of recurrent melanoma may include the following:

- Surgery to remove the tumor.
- Radiation therapy as palliative therapy to relieve symptoms and improve quality of life.
- Palliative treatment with biologic therapy.
- Hyperthermic isolated limb perfusion.
- A clinical trial of biologic therapy and/or chemotherapy as palliative therapy to relieve symptoms and improve quality of life.

INTEGRATIVE THERAPY

4. THE SCIENTIFICALLY FORMULATED AMINO ACID THERAPY

(Keep in mind, CAAT is much more than just a “diet”; it is an amino acid, carbohydrate, & glucose REDUCTION protocol which strategically uses the chemical reactions of amino acids, foods, and nutritional supplements to impair the development of cancer cells, thus starving them to death.) *Clinical*

trials have already been done with humans using amino acid deprivation formulas, and with much success. (Journal American Medical Association. 1967; 200:211)

CAAT is a course of therapy to control a patient's amino acid intake. This is achieved by taking certain foods out of a persons' daily food plan for a short time and by replacing them with a scientifically supported formula of amino acids. It is also important to emphasize that the food plan that accompanies the amino acid formula needs to be followed so not to offset any of the benefits we are creating by depriving the cancer cells the nutrients they need to grow. Also, it is important to realize that the patient does not need to abandon their conventional cancer treatment, (surgery, chemotherapy, radiation, hormone treatments) nor is it recommended that they do so unless it has already failed them. CAAT works synergistically with chemotherapy and/or radiation to enhance their benefits (see study by Dr. Marco Rabinowitz of the National Cancer Institute). His report on amino acid deprivation, such as with Controlled Amino Acid Therapy (CAAT), proven to inhibit phosphofructokinase which shuts down the energy supply to cancer cells, simultaneously enhancing the benefits of chemotherapy while lessening their toxic side effects. CAAT has also proven to work successfully alone.

Phase 1: CAAT Formulation

The most important component of CAAT is the scientifically formulated amino acids. Based on the specific formula for each cancer, it consists of separate amino acids, citric acid, and small amounts of sodium benzoate. Each formula replaces most of the regular daily proteins found in meats, dairy, fish, beans and nuts, which cancer cells can derive their energy from. The CAAT formula taken two times per day will nourish the healthy cells while causing the cancer cells to starve to death. Of course each individual has specific needs concerning their diet, and this is explained in the second phase of the protocol as well as with a specialist at the Institute when beginning the CAAT therapy.

Phase 2: Daily Food Intake

DISCLAIMER: The following food program **SHOULD NOT** be consumed without the amino acid formula and without consent from your doctor and our Institute.

Breakfast:

*1/2 Grapefruit **or** 1-orange **or** 6-ounces of fresh orange juice.

Whey Enhanced Protein (Vanilla Flavor – Vitamin Shoppe Brand) approximately 10 – 12 grams of protein – read label carefully, based on 150 lb. person].

A serving of Grits (Butter, cinnamon and other spices are okay).

1 cup of green **or** black tea (Fructose is sweetener of choice).

*** Do Not have ½ grapefruit if taking Chemotherapy**

Explanation: ½ Grapefruit **or** 1 orange **or** 6 ounces of fresh orange juice are rich in the natural nutrients called Limonene and Citric Acid. Limonene helps shut down the Ras cancer gene which is over active in 90 percent of all cancers. Citric Acid helps shut down glycolosis which in turn helps starve cancer cells to death.

Whey Enhanced Protein (Vanilla Flavor – Vitamin Shoppe Brand) Phosphorus is a nutrient that cancer cells must utilize in order to grow and reproduce. This brand of whey protein is very low in phosphorous and contains no additional vitamins, so when using approximately 10 – 12 grams of protein per 150 lb. person, it helps to protect normal cells, maintain a normal appetite, and also helps to fight edema. (Edema is the swelling or water build up in the legs or other sites in the body)

Whey protein is included in the daily menu of all advanced or metastatic cancer patients. When treating cancers that are stable or have regressed in size, patients then have the option of including other protein foods at their breakfast meals such as cottage cheese, yogurt, or soy foods. Eggs are allowed in the diets of patients with lymphoma and brain cancers.

Grits **or** Cream of Wheat **or** 1 slice of white toast **or** ½ plain bagel **or** ½ English muffin (Butter is okay)

Grits or white rice is the preferred carbohydrate food at each meal. The other choices are options once the patient's cancer is stable or reduced in size. Unrefined carbohydrates are included in the CAAT menu instead of whole grains to deprive cancer cells of a certain B-complex vitamin called Pyridoxine (Vitamin B-6). Cancer cells require this vitamin to manufacture certain amino acids that we keep away from through CAAT's amino acid reduction formula and diet. Grits is the preferred carbohydrate food at all meals instead of rice, corn, or pasta because it helps deplete Tryptophan in the body, which is essential for the growth and spreading of cancer cells.

1 cup of green **or** black tea, using fructose as the sweetener of choice. These teas are rich sources of several compounds that help shut down glycolosis and cut off the energy supply to cancer cells. Also, green or regular tea helps to prevent certain hormones and tumor growth factors from stimulating cancer cells to grow and metastasize to other parts of the body. Brassica teas can also be taken because they contain sulphorane, a nutrient that inhibits cancer growth, and also shuts down the cancer genes.

* Why we use fructose as the sweetener of choice will be explained in detail at the end of this phase of the CAAT protocol.

Lunch:

Amino acid formula (**4 level plastic scoops**) mixed with any of the following: Water & Fructose; Sugar free Kool-Aid; Diet ginger ale; Fresh lemonade & Fructose; Chicken or Beef broth; V8 juice.

Generous amounts of One cooked vegetable **or** a combination of the following: asparagus, broccoli, cabbage,

brussell sprouts, spinach, squash, string beans.

One serving (1/2 cup) of fresh fruit. Choice of: pear, orange, blueberries, raspberries, strawberries.

1 serving (moderate) of grits **or** corn **or** rice **or** pasta (Add tomato sauce or butter)

1 tablespoon of coconut oil

8 to 10 black or green olives

2 tablespoons of vinegar (minimum of 5% acidity) add to vegetables or food

1 cup of green **or** black tea (Fructose as desired)

Explanation:

This Amino Acid Reduction Formula (**4 level plastic scoops may vary**) combined with the special diet, allows the CAAT Protocol to reduce certain amino acids in the daily diet of the cancer patient, and is designed to replace most of the animal protein in the diet. Cancer cells require the amino acids glycine, serine, glutamic acid, and aspartic acid to synthesize DNA, build new blood vessels or duplicate its entire contents of proteins. Also, cancer cells require these and certain other amino acids in order to synthesize other proteins that act as growth promoting hormones or tumor growth factors. CAAT impairs the synthesis of a protein called elastin, which is absolutely essential to the manufacture of new blood vessels. The Amino Acid Reduction Formula, diet, certain phytochemicals and herbs work efficaciously to attack cancer cells at each and every biological front.

The generous amounts of one cooked vegetable or a combination of such helps keep normal cells healthy. They are low in carbohydrates and proteins, and high in phytochemicals, compounds which help fight cancer. Patients are allowed to eat these vegetables and salads whenever desired.

The 8 to 10 olives are rich in squalene and oleic acid, nutrients that have been reported to inhibit certain cancer growth factors. The calories in olives also help control body weight and increases ketones in the blood. Ketones help fight cancer by impairing glycolysis – a process in which cancer cells depend almost exclusively upon for their daily supply of energy. Vinegar (and fructose) are two natural products that increase the production of both **ACETIC ACID** and **CITRIC ACID** in the body.

Acetic acid and citric acid also help fight cancer by shutting down the process of glycolysis.

Normal cells derive most of their daily energy supply from acetic acid and citric acid, where as cancer cells derive most of their daily energy from glycolysis.

Dinner:

Amino acid formula (**4 plastic level scoops**) mixed with any of the following: Water & fructose; Sugar free Kool-Ade; Diet Ginger Ale; Fresh lemonade & Fructose; Chicken or Beef broth; V8 Juice.

Generous amounts of One cooked vegetable or a combination of the following: asparagus, broccoli, cabbage, brussel sprouts, spinach, squash, string beans.

One serving (1/2 cup) of stewed plums with fresh cream & fructose; use 4-ounces of orange juice if plums are not in season.

Avacado salad with lettuce, tomatoes, celery, onions, with lemon juice and coconut oil **or** olive oil.

2 tablespoons of vinegar (minimum of 5% acidity) add to vegetables or food.

1 serving of grits **or** corn **or** pasta **or** rice (Add garlic and butter or tomato sauce)

1 cup of green **or** black tea (Fructose as desired)

Mid Evening Snack: Ketogenic Cocktail – 2 ounces of fresh cream, ½ ounce each of both coconut & olive oil, 1 tablespoon of Fructose.

Sugar free Jell-O with whipped cream & Fructose **or** 1 plum **or** 4 ounces of orange juice.

Explanation: The sugar free jell-o helps to appease the appetite. Plums contain quinlic acid, which is converted into benzoic acid in the body and which in turn helps to deplete the availability of the amino acid Glycine (Glycine is essential to the synthesis of DNA for cancer cells) and the proteins that cancer cells require to build new blood vessels and their tumor growth factors. If underweight take two ounces of light cream and one ounce of olive oil/coconut oil as needed to maintain weight.

Optional Meal:

3 to 4 ounces of Veal, Fish of choice, Beef, Chicken breast, and 1-slice of white bread.

Consume this meal with a minimum of 3 hours before or after taking the amino acids.

Explanation: If the patient is 10 or more pounds underweight or if their albumin levels are below normal is when the optional meal is allowed. This meal should be eaten a minimum of 3 hours before or after taking the amino acids. CAAT provides sufficient protein to maintain the health of normal cells and adequate amounts of calories to maintain desired body weight. Any proteins taken in excess of amounts recommended in the diet will counter act the benefits of the CAAT protocol.

Special Diets: A special diet will be created for any cancer patient whose ability to consume food and liquids has placed them in a critical situation. When a patient is using a feeding apparatus, or they have become too weak or lethargic to eat and drink the daily minimum amount for survival, we will break up the total breakfast, lunch, and dinner over a period of every 2 hours during the entire day until the patient is capable of returning to a daily diet as

outlined above.

Carbohydrate and glucose reduction in this diet: CAAT'S dietary menu provides approximately 20 percent of its calories in the form of carbohydrates. Calories need not be a focal point or counted daily. It is recommended that all patients combat their cancers by keeping their body weight at normal or slightly below normal levels. A patient's desired body weight is regulated by their rate of metabolism, which in turn is regulated by their blood levels of thyroxine, cortisone, insulin, and the amounts of fats and oils in the diet. Studies with human cancer patients and laboratory animals show that reducing the calories of carbohydrates (glucose) in their daily diet by only 10 percent reduced the size of cancerous tumors. When carbohydrate (glucose) calories were reduced 40 percent, the cancers disappeared. It is recommended that those patients who are obese gradually and systematically lose their excess weight to increase the efficiency of the CAAT protocol. Those patients who are underweight shouldn't gain weight unless they are more than 10 pounds below normal levels. When a patient is underweight due to anorexia or cachexia, such illnesses must be addressed before the CAAT protocol can begin.

Why we use Fructose and Vinegar to treat cancer:

Nobel Prize winner Dr. Otto Warburg discovered more than 50 years ago that all cancer cells produce inordinate amount of lactic acid but he couldn't explain why.

In 2001 our Institute published the first study to show that cancer cells produce excess amounts of lactic acid because they could not access the oxygen in compartments in the cells called the mitochondria. This provided evidence that cancer cells depend almost exclusively upon glycolysis or the metabolism of glucose as their major source of energy.

Dr. Spitz and Dr. Lee with other cancer researchers published studies showing that when cancer cells are deprived glucose, their energy supply is cut off which causes these cancer cells to commit suicide.

Therefore shutting down glycolysis would be one means of destroying cancer cells because energy can only be derived from glucose through the metabolic process called glycolysis.

Recently our Cancer Institute discovered that both acetic acid and citric acid could inhibit the activity of a key enzyme in glycolysis called phosphofructokinase, which in turn shuts down the process of glycolysis. Our cancer Institute is the first to introduce both fructose and vinegar as treatments for cancer because they either contain or produce acetic acid.

In conclusion, fructose and vinegar are added as supplements to the CAAT protocol because of their acetic acid properties that help shut down glycolysis, shutting off cancer cells energy supply and causing them to die off.

Phase 3: Nutritional Supplements

Nutritional supplements are based on each unique situation. For example, slow growing cancers produce low levels of toxic free radicals. Tumor cells that grow aggressively produce large amounts of toxic free radicals. The patient will be instructed whether or not to take anti-oxidants (in a nutritional supplement) and at what dosage, according to the levels of toxic free radicals produced in the cancerous cells.

An example of how nutritional supplements can help manipulate cancer cells involves vitamin B-6 (pyridoxine) There are four amino acids essential to the synthesis of DNA. However, those amino acids cannot be synthesized without a certain enzyme, which includes vitamin B-6 among other components. Any supplement containing vitamin B-6 **SHOULD NOT** be taken during the first 2 months of the CAAT protocol.



The patient will be instructed as to which nutritional supplements or phytochemicals should be purchased and at what dosage strength. Keep in mind that each supplement only complements the CAAT protocol. However, when they are combined they augment the therapeutic benefits of the aminoacid, carbohydrate, and glucose reduction diet.

Parsley: Contains ingredients that can help shut down certain enzymes called Epithelial Growth Factors, which stimulate the growth and spread of cancer. (CAAT'S amino acid reduction diet works in the same manner)

Vitamin D: Helps activate in many kinds of cancers enzymes called Phosphatases, which literally shut down the activities of other enzymes called Kinases, which are essential to the growth and reproduction of cancer cells.

Green Tea Extract: Phytochemicals in tea help shut down glycolysis (cancer cell's main supplier of energy) and thereby help to starve cancer cells to death. These effects help complement the effects of CAAT'S carbohydrate reduction.

Anti-Oxidants: The controversy as to whether or not to treat cancer with anti-oxidants is slowly resolving with the current understanding of how they affect the activity of genes and enzymes in cancer cells. The prevailing data shows that the benefits or lack of benefits depend upon the oxidative state the cancer cells are in. Anti-oxidants taken when the cells are in a very high oxidative state may prevent cancer cells from entering apoptosis (

apoptosis is when a cancer cell commits suicide) When oxidative stress in cancer cells is only slightly above normal, anti-oxidants are then expected to stop their growth and reproduction.

Blood Chemistry: Blood tests are usually taken every 6 to 8 weeks, depending upon the results of each test. Not only is it important to monitor the tumor markers but equally important to keep abreast of the overall health of normal tissues and organs. For example, it is important to learn of the health of the kidneys and liver, whether the body is producing sufficient red and white blood cells, etc. Low albumin levels most often indicate insufficient intake of proteins in the diet and this problem would have to be addressed. CAAT is designed to attack cancer but keep the normal cells and tissues functioning harmoniously.

Whey Protein: This protein food is recommended at the breakfast meal to help meet the daily needs of amino acids for the normal cells of the body, and to help keep albumin levels normal and to help prevent edema. We recommend Whey protein purchased from the Vitamin Shoppe because it is the only brand that we have seen with no phosphorous or additional vitamins added to it.

Grits: Grits are also recommended at the breakfast meal in place of whole grains because it is low in vitamin B-6. Cancer cells require B-6 to manufacture the amino acid Glycine, which is required for DNA synthesis. Grits, instead of whole grains, therefore helps prevent cancer cells from manufacturing DNA and building new blood vessels.

Calcium D-Glucurate: This phytochemical helps the body to retain a compound called Glucuronic acid. This is necessary to eliminate both estrogen and testosterone from the body. This is why Calcium D-Glucurate is added to the regiments of patients with breast & prostate cancers. Calcium D-Glucurate is not to be confused with calcium carbonate, which is nothing more than a calcium supplement.

D-Limonene: This phytochemical found mostly in citrus fruits blocks the process called Isoprenylation, which is necessary for tumor growth factors such as the RAS gene, Epithelial Growth factor, Tyrosine Kinase, and Insulin-Like-Growth-factor, to send their signals into the nucleus of a cancer cell and directs them to grow and divide into more cancer cells.

Tocotrienols: This member of the Vitamin E family also helps shut down Isoprenylation and assists D-Limonene in blocking the actions of the various tumor growth factors. More specifically, tocotrienols shut down an enzyme called HMG-2, which is essential to the synthesis of the building blocks that form the Isoprenylation process.

Niacin: This B-Complex vitamin works with D-limonene and the Tocotrienols to shut down the process of Isoprenylation, which as mentioned above prevents the cancer promoting RAS genes from sending signals into the nucleus of the cell. Niacin also helps deplete the amino acid Glycine, which cancer cells need to synthesize DNA. And by reducing cholesterol in the body, Niacin helps lower the production of estrogen and testosterone.

Choline: This B-complex vitamin is included in our supplement list to help the liver metabolize Niacin and other compounds and to help fight fatigue that accompanies most forms of cancer.

Selenium: Numerous studies show that this mineral can interfere with the activity of certain genes that promote the growth of cancer and to induce cancer cells to commit suicide (apoptosis)

Perilla Oil: This oil is rich in Alpha Linolenic Acid which can inhibit the growth of cancer cells in several ways. One way is to inhibit the synthesis in the body of a tumor growth promotin hormone called Prostaglandin-2, also, Alpha Linolenic Acid inhibits the actions of certain genes that promote the growth of cancer cells. Linolenic acid is not to be confused with linoleic acid, which is a bad fat that stimulates the growth of cancer cells. This bad fat, linoleic acid, is found in all vegetable oils and nuts (With the exception of coconut oil). Olive oil has the least amount of this bad fat.

Super Miraforte: This herb impairs the synthesis of estrogen from testosterone in the body and is included in the regiments of women with breast cancer.

Licorice Root Extract & Pantothenic Acid: This herb and vitamin are added to the regiment when it is desirable to produce steroid like actions in the body. Also used to help patient's gain weight and to inhibit the growth of lymphomas and leukemia's.

Resveratrol: This phytochemical blocks the actions of a number of a number of cancer promoting genes thereby causing cancer cells to enter into apoptosis (cell death) and is included in the treatment of all cancers.

Indole-3 Carbinol & D.I.M.: These two phytochemicals block the actions of both estrogen and testosterone and are included in the regiments of both breast and prostate gland cancer.

Melatonin: Numerous studies show that this hormone blocks the synthesis of the cancer promoting chemicals in the body called Leukotrienes, and is included in the treatment of all cancers.

Artho Pro System: This combination of herbs and phytochemicals inhibits the synthesis of the cancer promoting hormone called Prostaglandin-2 and the Leukotriens and replaces the drug celebrex when liver problems are present. The Prostaglandin hormone is over active in most cancers and stimulates cancer growth. The body manufactures the Prostaglandin hormone from the bad fat, Linoleic acid, mentioned above.

Licorice Root Extract & Pantothenic Acid: This **HERB** and **VITAMIN** are added to the regiment when it is desirable to produce steroid like actions in the body. Used also to help patients gain weight and to inhibit the growth of Lymphomas and Leukemias.

CAAT is designed to attack cancer, while keeping normal cells and tissues functioning harmoniously.

*** When considering any type of complementary cancer treatment or alternative cancer treatment, always consult with your physician first, as possible interactions could reduce your regimen's efficacy.**

If this information has generated any questions you would like answered.

[Questions? Click Here](#)