Cancer’s Unwritten Law

There is an unwritten law (Coscarelli’s Law) about cancer and its treatment that goes like this: “For every physical effect, there is an equal reactive psychological effect.” It seems so obvious when you say it out loud but is so hard to realize when you are in the midst of a cancer diagnosis, diagnostic work-ups and treatment regimens. So I often find myself explaining this unwritten law and its details to patients, family members and the physicians that treat them. From the moment the word “cancer” is uttered, life changes, not because in that instant the world actually deconstructs, but because it psychologically changes you and how you think and feel about life at all levels. It also changes how your family and/or a close network of friends think and feel.

Think for a moment about the myriad of physical situations that a person diagnosed with cancer begins to experience. Almost every test requires cognitive energy for scheduling appointments, dealing with insurance companies and inevitably some type of discomfort from needle sticks, dyes injected, hard cold tables, unusual or uncomfortable positions, and placement in rooms in the center of a cylindrical tube that goes rat-a-tat-tat at various deafening levels. There are more visits to more doctors, requiring more time and attention being directed to health issues instead of other activities such as work, family and social networking. When treatments begin there are inevitably more pills to swallow, IV’s to be started, blood tests to be taken, surgeries to have and side effects to be endured. It is not simply the pain and physical discomfort of these with which patients must grapple, it is the psychological impact as the mind processes each of these events and the ripple effect that they have across the fabric of a person’s life. While one event seems manageable, the sheer number of discomforts, physical changes, and daily appointments add up and can snowball into something that, at times, seems overwhelming. I’m not even outlining the deeper existential issues of life, death and meaning yet!

How one responds psychologically to these events is highly individual. What may seem like a non-event to one person can be monumental to another. Each individual’s personal history, experience preceding the diagnosis as well as the details about the individual’s treatment and cancer makes each person’s experience a very personal journey. That being said, we have documented a number of the most frequently expressed reactions and feelings. It is not unusual for patients—and we must also add family members—to react with anxiety, depression, and sadness. The uncertainty of situations, the waiting for information, the twists and turns that the diagnosis and treatment can lead people through varies by individual and, as a result, the cancer journey is uniquely personal. Despite this, there are documented experiences that fit within what we can call a “frame of normalcy.”

One of the most common reactions that people report is worry about what will happen in the future as they face the uncertainty of cancer and its treatments. For most people, you are traveling unfamiliar territory and with this comes anxiety about the process and the outcome. Often the experiences of getting treatments and tests are new, bringing anticipation about what it will be like and how to deal with the process. For patients who have had few medical experiences, these anxieties can be significant. For those who have had more exposure to the medical system, the veteran experiences may help them feel more comforted, but only if their previous experiences were ones in which they felt well cared for and there were no traumatic experiences along the way. A history of negative experiences with a health care team, treatments, or prior procedures, can actually increase fear and anxiety as they retrigger previous trauma or create anticipation about the repetition of new traumas.

Anxiety is just part of the picture. Cancer changes things in small and large ways. These changes are characterized by feelings of loss. While people are accustomed to the concept of loss and grief when a loved one passes away, they are often unprepared for the feelings of loss and grief that can come from the day-to-day changes brought about by cancer. When a cancer diagnosis is made, you lose your sense of health as previously known. There may be losses of time for cherished activities such as work and family life, loss of hair, loss of bodily functions or even the body as it was formed prior to surgeries. Life may go on for a very long time after a cancer diagnosis, but that does not mean that the individual is not faced with a series of losses and gains.

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of losses that must be psychologically processed, managed and experienced. Grief is a normal reaction to loss and it can be experienced in a variety of ways such as sadness, tearfulness, a feeling of heaviness or cognitive impairment (e.g., not thinking clearly, forgetting things, feeling disoriented or discombobulated). It is normal to have these feelings and important to know what they represent. Sometimes sadness and loss can give way to depression which may have more serious psychological consequences. Depression may develop as these losses mount, if the treatment process is protracted or there are ongoing changes not being able to live your ordinary life can cause great grief.

Cancer inevitably causes disappointments and frustrations. These feelings can come from something that seems simple to healthcare providers, such as a cancelled or postponed appointment, long waits to see the doctor, difficulties with the insurance company or approvals, an unpleasant or insensitive nurse, or being unable to find a parking place. Disappointments and frustrations can come from inadequate treatments, inconvenient or difficult side effects, protracted healing, complications from and especially failures of treatment. Even those individuals who are attempting to be supportive can make statements that seem insensitive. Patients sometimes feel that their needs are not met by any number of individuals upon whom they have become dependent for emotional and physical support in the regulation of their environment or at home. These are also forms of loss as expectations may not be met and these disappointments must be absorbed along with the onslaught of other challenges.

Cancer also can affect your psyche in relation to your spiritual belief system as it may raise deeper questions of concern. It is common for existential issues to arise. These may not be based in formal religion, although they can be. Patients may question their beliefs, their sense of purpose and meaning in life, the role of suffering as well as their qualitative beliefs about God’s presence or absence. These questions may arise through the process of loss and acceptance of change. Suffering can be a source of stress or distress. However, being able to make meaning of your experience can often serve as part of a healing process.

All of these events are cumulative and form a basis of stress for the patient and the family. The build-up of stress can seriously affect mood, energy and vitality as well as your sense of purpose and meaning in life. The role of suffering as well as their qualitative beliefs about God’s presence or absence. These questions may arise through the process of loss and acceptance of change. Suffering can be a source of stress or distress. However, being able to make meaning of your experience can often serve as part of a healing process.

1. Learn a relaxation skill and utilize it every day.
Relaxation exercises can take many forms ranging from deep breathing, progressive muscle relaxation, to combinations of these with guided imagery. They can be learned through books, videos, workshops or classes. The Center has a meditation class that teaches several of these different techniques and guarantees practice at least once per week. If all the techniques are available to patients, this is by far one of the best researched and most beneficial tools and should be incorporated into all patients’ and families’ skill sets for managing the effects of cancer. Relaxation exercises practiced regularly can reduce the cumulative effects of stress and raise a person’s threshold in combating the inevitable stresses in the future. It can affect mood in a positive direction, reduce anxiety and lead to an overall sense of well-being. This is the single best thing a patient can do to mitigate the psychological consequences of a cancer diagnosis. Not every technique resonates for individuals, so finding the best fit is an important goal.

2. Learn mindfulness.
Mindfulness is the process of being aware of the moment-to-moment experiences of life. It helps patients and families become grounded in the present moment rather than dwelling in the past or worrying about the future. It requires practice and is best learned in a group environment. There are multiple resources on the internet, through classes in the Center and around the country. There is an entire program at UCLA devoted to this important tool called the Mindfulness Awareness Research Center (MARC). We have a group dedicated to Mindfulness for our patients that meets weekly.

3. Identify and utilize soothing and restorative practices.
Different people will find different techniques soothing and/or restorative. Some of the common ones that benefit patients and family members are massage, acupuncture and acupressure. These integrative techniques can help bring calm, release tension and build the body’s strength to cope with stress. Relaxation exercises and mindfulness practice can also be included in this category.

4. Exercise!
Exercise has so many psychological and physical benefits. The psychological health and immunity 11 years later showed a significant benefit in overall survival curves for those patients who received the comprehensive intervention. The comprehensive intervention, conducted by a psychological team, taught patients about stress and its impact on coping, provided patients with a relaxation tool called progressive muscle relaxation, helped them learn how to eat a healthy diet, included exercise such as walking throughout the treatment and recovery phase, facilitated communication skills with the medical team and taught patients about symptom management. There are additional studies that have shown the benefits of mindfulness, psychotherapeutic interventions by psychologists and oncology social workers, exercise, and contact with a social network. In short, what this tells us is that medicine alone is often not enough when it comes to cancer. Instead, patients and family members need a comprehensive approach. Below is a list of antecedents that patients can incorporate into their routines that, when implemented together, form a comprehensive approach to physical, psychological and spiritual wellness.

5. Maintain contact with your social network.
Sometimes the losses caused by cancer and the drain on your discretionary time limits how much contact you can have with loved ones and friends. While your energy level may impact your ability to engage, it is essential that you maintain your social contacts. Everyone needs at least one person that they can confide in through the process. Social contact acts as a buffer to the stresses of the disease. It is also a distraction from the discomforts. Close family and friends can help insulate you from the psychological impact of the disease and often provide a sense of meaning and purpose. Do not isolate yourself. If energy is the issue, reduce the amount of time spent with your friends and family but do not postpone those contacts for better days. Even if social networking through the computer may be an important way of maintaining contact, do not limit your interaction to a “screen.” Social contact needs to be three-dimensional and involves all the senses. Touch and be touched are all healing elements. Think of social contact as important to you as your medicine.

6. Recreation.
This is an old word for the process of having fun. For anyone touched by this disease, cancer is not fun and dealing with it is not a fun time. It has a way of crowding out the activities that brought enjoyment into your life and replacing them with tedious, medically oriented and often uncomfortable tasks. If you are dealing with reduced energy and physical capacity recreation can include quiet and simple activities. It can be reading a novel, talking on the phone, playing a game of cards or a board game. It can be working in the garden or, if your energy is diminished, sitting in the garden watching others pull the weeds, plant and chat. It can be a shared cup of tea. It can also be surfing, playing basketball, running or swimming. Think back to pre-cancer days, even to childhood times. Remember what brought you enjoyment and make sure that you make an appointment with yourself to recreate for the purpose of joy. Joy is a tremendous antidote to the psychological consequences of cancer!

7. Manage your symptoms.
Sometimes you have to live with your symptoms, but you should never give up actively trying to moderate them. Pain is a common symptom that creates psychological distress. Pain should be addressed with your physician; if it cannot be resolved you should seek out consultation with a pain management or palliative care specialist. Other physical symptoms such as nausea, vomiting and difficulty eating can diminish your quality of life and need to be managed. Fatigue and energy can be problematic and need to be assessed. Sometimes these can be exacerbated by depression. Sometimes integrative medicine approaches complement your traditional medicine and can be helpful in symptom management. The Center offers educational services from an integrative medicine physician who can help patients customize wellness approaches to alleviate these ongoing and often nagging problems.
8. Seek out qualified psychological care.

Do not underestimate the importance or value of psychological support during cancer and its treatments from a professional, such as a psychologist or clinical social worker. These individuals have knowledge and skills that can help patients look at their circumstances from a different perspective, acquire coping strategies and even develop a comprehensive plan. Our Center has clinicians dedicated to providing psychosocial help. It is effective and beneficial for patients and families and can help with processing loss, managing anxiety, addressing sadness and depression and helping develop a psychological stance to cancer that allows for change and adaptation. Just because you never needed this in the past does not mean that you will not benefit from it now! The more experience the clinician has counseling patients about the cancer experience, the more they will be able to offer practical, effective and useful assistance. Cancer can change from a devastating experience to an impetus of great growth.


Mood changes such as anxiety, depression, persistent worry, as well as symptoms of fatigue and cognitive dysfunction can often be mitigated by the addition of specific medications prescribed by a psychiatrist. Many patients benefit from a consultation to evaluate whether these specific groups of medications might relieve some of the impact of the psychological consequences of cancer. These medications can improve quality of life and help you have the energy and mindset to embrace the other wellness-oriented strategies presented in this article. The Center has a psychiatrist well versed in cancer treatment and its consequences who can assist patients and families with decisions about these medications. While many physicians will routinely prescribe an anti-depressant or anti-anxiety medication, I strongly advise that you have a specialist evaluate the patient and make recommendations based on expertise with psychiatric medication. It often leads to a better match between medication and need, as well as appropriate dosage adjustments and minimized side effects, which are important in the success of this type of care.

10. Quest for meaning.

Connecting to that which is meaningful in your life is often a strong antidote to almost all discomforts. For some that quest may be easy and tangible, perhaps something from a particular religious practice. For others, it may be less apparent and may require some soul searching. Meaning is not always religious or even identified as spiritual, but rather the one thing that makes life feel valued. Having discussions with trusted individuals who are used to addressing these issues can help to form a perspective that provides strength through the cancer journey.

At the Center our psychologists, social workers and chaplain frequently help patients and their family address these existential questions. It is not unusual for individuals to find some gifts along the way, which include re-setting of priorities, greater meaning in relationships to loved ones or connections to them, appreciation for simple things or feeling grounded in a sense of purpose. Whatever that is for each individual, it is important to give yourself time to reflect and experience what is meaningful for you.

Being able to set realistic goals and expectations is an important aspect of the adaptive process. It requires concrete information about likely events and a willingness to consider the range of possibilities. Sometimes it is hard to set realistic goals because it means accepting a reality that is different than what you really want to accept. This can lead to distress and frustration along the way. All of this requires a high degree of flexibility at a time when flexibility can be compromised by stress. Keep in mind that with cancer you are in an ever changing landscape and that what is present in this moment will likely change. Being open to change, processing the full range of emotions that go along with it, and integrating new solutions to new problems is essential. Positive growth through the cancer experience is even possible. Keep in mind that positive growth does not require a positive attitude; you should not expect to have a positive attitude all the time and beware of those who insist that this is the only way or even very important. Being able to tolerate and experience the psychological discomforts creates an opportunity to learn and grow personally, allowing adaptation and evolution in one’s emotional development. It is rare to see someone who is not changed in some way by the cancer experience. I have encountered many patients who say that though they would not have chosen this pathway they would not undo the wisdom, growth, and strength that they obtained along the way.

I wish each of you on this journey the opportunity to experience healing and growth as part of the myriad of psychological effects caused by the physical effects of the disease and its treatment.

Anne Coscarelli, PhD

a comprehensive approach to physical, psychological and spiritual wellness.
Acupuncture, part of Traditional Chinese Medicine (TCM), has been in existence as a treatment modality for a very long time. It was used in China, Japan, and Korea, among other locations, over 3,000 years ago. Approximately 200 years ago its popularity grew in Europe. CAM, which has been used around the world for thousands of years, was the only source of medicine for most societies. What we call “mainstream” or allopathic medicine is a relatively new discipline, in existence for only about 200 years. Integrative medicine, which is the practice of combining these techniques, is also a relatively new practice of modern medicine. Integrative medicine utilizes both traditional Western medicine and CAM approaches to treat conditions, symptoms and diseases. Cancer cannot be treated with a CAM only approach; it is an aggressive disease that will progress without the treatment of mainstream medicine. Acupuncture and other CAM approaches can be used to help improve the status of a patient, but should be combined with modern medicine to treat—inducing nausea, radiation, surgery and the newer targeted treatments. It would be considered irresponsible on the part of an acupuncturist or other CAM provider to tell patients that their cancer can be treated without these modern approaches.

Acupuncture stems from an Eastern philosophy that is based on the body having channels and meridians. There are 12 channels and approximately 1,500 points that can be used to stimulate the flow of energy which in traditional Chinese medicine is called “Qi.” In Eastern philosophy Qi flows throughout the body. When the body is in harmony the Qi flows freely; when the body is sick the energy, or Qi, is blocked. Patients with cancer often believe that Qi is blocked. The examination and assessment from a traditional Chinese medicine perspective is completely different than from the Western medical exam. The patient’s pulse is assessed from different sides of the body and locations and the patient’s tongue is examined. The bodily systems are divided differently as well, grouping organs and functions and overall conceptualizing it differently. It takes substantial training to learn the meaning of different traits seen on the tongue as well as how Qi is blocked.

The National Center for Complementary and Alternative Medicine (NCCAM) is a branch of the National Institutes of Health that is dedicated to conducting and supporting research, training researchers, and providing information about CAM. They divide CAM modalities into five major domains which are listed below with examples:

- **Alternative Medical Systems**
  - Traditional Oriental Medicine and homeopathy
  - Mind Body Intervention
  - Meditation, imagery, relaxation
  - Biologically-Based Treatments
  - Herbs, high dose vitamin therapy, enzyme therapy

- **Manipulative and Body-Based Approaches**
  - Massage, yoga, chiropractic
  - Energy Therapy
  - QiGong, Reiki, therapeutic touch

As you can see from the italicized examples, aspects of TCM approaches are included in each of these five different domains: Traditional Chinese Medicine, meditation, herbs, massage, and QiGong. An increasing number of patients with cancer are using complementary and alternative medicine. NCCAM estimates that 7-54% of patients with cancer use CAM and they often do not tell their physicians about these practices. Even higher numbers, 48-88% of patients who are being treated in comprehensively cancer centers in the United States, are purported to be using CAM approaches in conjunction with their mainstream treatment.

Few people question whether acupuncture can benefit a broad range of problems and disorders, but understanding how it works is sometimes difficult from a Western medical point of view. One study documented that the same areas of the brain would light up on a functional MRI when one of the acupuncture points related to the eye was stimulated; you should note that the acupuncture point was not located anywhere near the eye. When an irritating flashlight was flashed in the eyes of the person that same area of the brain lit up on functional MRI. This demonstrates that the acupuncture points that have been identified for specific parts of the body in fact are receiving information in the same areas of the brain as when the actual body part is stimulated. It is also believed that acupuncture is helpful with moods, hormonal imbalances and menopausal symptoms because dopamine, norepinephrine and endorphins—all neurotransmitters—can also be stimulated.

In 1998, an NIH consensus panel reviewed the literature on acupuncture and made the following recommendations about how it should be used. They stated: “Promising results have emerged, for example, showing efficacy of acupuncture in adults postoperative chemotherapy nausea and vomiting and in postoperative dental pain. There are other situations, such as addiction, stroke, rehabilitation, headache, menstrual cramps, tennis elbow, fibromyalgia, myofascial pain, osteoarthritis, low back pain, carpal tunnel syndrome, and asthma, in which acupuncture may be useful as adjunct treatment or an acceptable alternative or be included in a comprehensive management program. Further research is likely to uncover additional areas where acupuncture interventions will be useful.”

This United States consensus panel was the first to positively evaluate acupuncture as a successful modality to treating patients with cancer. Acupuncture is primarily used to assist with chemotherapy-related side effects such as myelo-suppression with leucopenia, thrombocytopenia and anemia, nausea, vomiting and mucositis (ulceration of the mucous membrane usually in the mouth). It is also recommended for dry mouth (xerostomia) caused by radiotherapy in brain tumor patients. Other aspects of symptom management for which acupuncture is used includes cancer pain, insomnia, fatigue, mood changes, loss of appetite, feeling of a loss of control and weakened immune system. Traditional Chinese Medicine is also used for menopausal symptoms caused by chemotherapy as well as chemotherapy-induced diarrhea or constipation, neuropathy, skin reactions, liver toxicity and end-of-life care. Acupuncture is utilized and can be helpful for pain management in patients with cancer and in other conditions.

When doing symptom management for conditions such as nausea or vomiting, it is important to first identify the cause of the symptom. Specific symptoms can sometimes be signs of conditions that need other treatments. CAM practitioners need to know when to diagnose and get to the root of the problem versus just masking it. Claims to “cure” cancer with natural and non-toxic treatments are inappropriate and not true. Some CAM providers will tell patients that chemotherapy is toxic; however, chemotherapy is often one of the most important treatment strategies for treating cancer. In addition, CAM providers need to know about herb-drug interactions as well as the interactions of CAM herbs that can be dangerous or even nullify the benefits of one over the other. For example, ginseng and green tea are often combined by the unknowing, but they actually cancel each other out when used together. Many traditional Chinese formulas have anywhere from 2 to 26 different herbs. It is important for patients to be aware of non-conventional treatments that may have untoward side effects associated with them and to assess the risk of harm versus the benefits. Non-conventional and unregulated treatments can present the potential for harm to the patient. All acupuncturists are required to have a state license. There is also an additional optional national license. Acupuncturists who work with cancer patients do well when they have general medical training as a background including hospital system experience. Nurses and physicians who combine East and West modalities are often the most knowledgeable because they can better understand the benefits of both. It is essential to have good communication skills to effectively work with and understand the needs of the patient as well as to communicate with the conventional Western medical team. Finally, an acupuncturist who is experienced working with oncology patients is better than one who has not focused on this particular area of care. There are special points that should be used with someone who has a cancer diagnosis. It is also important that the practitioner be familiar with the chemotherapy drugs when treating cancer patients with Chinese herbal medicine. Many of the more toxic anti-cancer herbs can interfere with chemotherapy, although most of these are also not allowed to be used in the United States.

Most importantly, the experience of acupuncture should lead to feeling better; acupuncture can be an important adjunct to cancer care and well-being.
SKIN CANCER: PREVENTION AND EARLY DETECTION

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This is summary of a lecture presented on April 12, 2011.

more than 2 million cases of skin cancer will be diagnosed this year in the United States alone. The three most common types of skin cancers are basal cell carcinoma, squamous cell carcinoma and melanoma. There are a few important risk factors for skin cancer:

- Having fair skin, blue/green eyes, and blonde/red hair increase the likelihood of developing skin cancer.
- Exposures to the sun as well as a history of sunburns are important factors as well.
- Individuals who live in sunny climates are most affected; Australia has one of the highest rates of skin cancer.
- Despite the strong lobbying force of the “tanning” industry, sunlamps and tanning beds are high risk factors; they do not make the skin healthier, but rather damage it.
- X-ray treatments that are given to the face for acne are also a risk factor, especially for basal cell and squamous cell skin cancers.
- Family history of skin cancer such as melanoma is an important known risk factor and should always be reported to your physicians.
- In addition, people who have had organ transplantation must take immune suppressing drugs and this places them at risk for skin cancers as well as other malignancies. UCLA has a special clinic for these patients.
- Diseases that weaken the immune system such as lymphoma and HIV are also risk factors.
- Exposure to arsenic (which has been found in high levels in some well water), coal and industrial tar are risk factors leading to skin cancer.
- Finally, there are a few rare genetic conditions such as xeroderma pigmentosum and Gorlin’s syndrome that increase the risk of specific types of skin cancer.

Basal Cell Carcinoma

Basal cell carcinoma is the most common cancer in the United States and comes from the base layer of the skin. It is hard to know how many actual cases there are because basal cell carcinoma is not considered a reportable cancer to central registries. Many dermatologists remove them and they are not counted.

Basal cell carcinomas tend to be slow-growing, although there are exceptions, typically in sun-exposed sites such as on the face, ear, and scalp. Basal cell carcinomas rarely metastasize to other regions of the body, although there are anecdotal reports of metastasis.

Squamous Cell Carcinoma

Squamous cell carcinoma is the second most common skin cancer in the United States. Like basal cell carcinomas, they commonly occur in parts of the body that are exposed to the sun such as the head and neck area, lips and ears. Squamous cell is most often seen in people over 50 years of age. It does have the potential to spread (form metastases) and can migrate to the local lymph nodes. Metastases are more common in immunocompromised individuals such as those who have had organ transplants. Squamous cell carcinomas tend to be more rough and scaly in appearance. Since they arise from the top layer of the skin they contain keratin. Some can grow rapidly. Actinic keratosis is a pre-cancerous skin lesion that should be treated before it develops into squamous cell carcinoma. Actinic keratosis is often treated with liquid nitrogen. The most common treatment for squamous cell carcinoma is surgical removal.

Melanoma

Melanoma, the third most common type of skin cancer, arises from the pigmented cells of the skin. The incidence of melanoma has been increasing for the past 30 years, especially among young Caucasian women ages 25-29 years of age. Approximately 75% of skin cancer deaths are from melanoma. If detected early and surgically treated, the cure rates are in the 90 percent range. If it spreads to the lymph nodes the five year survival drops to about 60%.

The most common factors for identifying a melanoma used to be called the ABC’s of melanoma; however, recently factors D-F have been added.

- “A” stands for “asymmetry of the lesion”: if you divide the mole or concerned area in half, they are not mirror images, rather they look different.
- “B” stands for “border irregularity”: the borders of the lesion are not smooth.
- “C” stands for “color variegation”: the color varies throughout the lesion. It may not be all one color but may have variations in intensity or coloration.
- “D” stands for “diameter”: it is usually larger than the head of a pencil eraser or 6mm and growing.
- “E” stands for “evolution”: it is important to know how a lesion has evolved and how it is changing. For example, a mole that has been on the body for a long time, suddenly begins to look different or change. Melanomas often just arise, from no other previous apparent mole. This is important to note and is a trigger to see a dermatologist.
- “F” is for “feeling”: does it feel different or is it symptomatic in some way such as bleeding. While less common, some melanomas are not pigment ed and so any sort of skin change needs to be evaluated.

Having a dermatologist really check your skin thoroughly from head to toe is an important screening method for early detection. Melanomas can show up in hard to see areas like your scalp, buttocks (between the cheeks), and bottoms of your feet as well as in more visible places. If your skin checks are not this comprehensive, then you are not being adequately screened for this type of skin cancer. Remember, melanomas do not always appear in sun exposed areas.

Prevention

Most people know that skin cancers require protective habits, including: seek shade, avoid sun exposure between 10am and 4pm, wear broad brimmed hats that have a wide brim, put on sunglasses, cover up with clothing (tighter weave is better) when possible and use broad spectrum sunscreen which should be reapplied every 1-2 hours. Sunscreen is a third line of defense and cloth ing come first. Finally, never use tanning beds. It is important to protect your children in all of these ways. Ultraviolet (UV) rays are not good for your skin. UVB rays have longer wave lengths and can go through glass. UVR rays have shorter wave lengths and are usually blocked by glass. UVA rays cause immune suppression, premature aging and age spots. UVR rays cause sun burns. Eighty percent of the sun’s UV rays can pass through clouds, so you are not protected even on a cloudy day. When you are outside you should also be aware that sand reflects 25% and snow reflects 80% of the sun’s rays. In addition to 100% of the rays that you get directly from the sun, you get additional exposure from the rays that are reflected back upward onto your body by these surfaces.

Many people ask which is the best sunscreen to use? My answer is “the one that you are going to wear!” If you do not put it on, it just does not help. Whatever sunscreen you choose should be used regularly, so make sure you like it enough to use it. An important technical factor to consider is that your sunscreen will only protect you for a certain amount of time. Sunscreens usually have several different chemicals, some protect against the UVA rays and others protect against the UVB rays. Physical blockers contain zinc oxide or titanium oxide and they block both UVA and UVB rays. Sunscreen must be reapplied regularly especially after swimming or perspiring heavily. Sunscreens are required by the FDA to have an expiration date. Most people do not put on enough sunscreen. You should use it generously and it is best if applied half an hour to an hour before you go into the sun.

Summary Highlights

- Protect yourselves from sun exposure.
- Avoid tanning beds/booths/salons.
- Get regular and thorough skin examinations.
- Do not ignore changing or symptomatic skin growths or moles.
- Have a small skin sampling or biopsy to confirm a diagnosis.
- Remember, skin cancer has a high cure rate if detected and treated early.

[Editor’s note: The Reflections Boutique in the 200 UCLA Medical Plaza, suite 163 provides a range of skin care products and hats that can be used to protect the skin. All sales in this boutique support the many free psychosocial support and educational services offered to patients with cancer and their families in the Simms/Mann — UCLA Center for Integrative Oncology. For more information, go to www.SimmsMannCenter.org or call Reflections directly at 310 794-9090.]
Breast cancer is the most frequently diagnosed cancer worldwide. With 1.38 million new cases diagnosed each year, it continues to be the leading cause of cancer death for women. Half of all breast cancer diagnoses and 60% of deaths occur in economically developing countries. The rates are high in Western/Northern Europe, Australia/New Zealand, and North America and differ due to differences in reproductive/hormonal factors and availability of detection services. In the United States, African-American and Latina women have lower breast cancer detection rates than Caucasian women with breast cancer, likely resulting from a lack of access to appropriate screening strategies as well as the more recent understanding that these populations have different subtypes of breast cancer. Early detection decreases survival rates for all populations; thus, screening procedures continue to be an important strategy.

A Shift in Classifying Breast Cancer

A major shift is occurring in how scientists classify cancers, particularly breast cancers. In the past, tumors were classified by how they looked under the microscope and their organ of origin. Rudolf Ludwig Karl Virchow (1821-1902) developed this classification system for cancer in 1863. Since that time, medical students have memorized what has been an enduring paradigm that is only now shifting. In this paradigm, 70-80% of all tumors were defined as infiltrating ductal carcinoma, a definition which provided little understanding about the wide variability of outcomes for patients with this diagnosis, and offered no information about treatment. Today, tumors are classified based on their molecular structure. Each cancer cell has a distinctive pattern in which some genes are turned on while others are turned off. These distinct gene array patterns have been identified and to date there have been five subtypes of breast tumors defined: basal-like, Her2/neu+, Lumin B, Lumin A, and Lumin C. This shift in classifying breast cancers is leading to a major change in breast cancer treatment. In the past, tumors were treated with chemotherapy that kills all rapidly dividing cells. Now, research is directed at tumors being treated with therapy that is rationally targeted toward the molecular defect in tumor cells, thus leaving normal cells alone. This targeted treatment means that we must determine the underlying biological reasons for the cell malignancy to allow for sub-classification of tumors based on molecular abnormality. We must know more about the details of how cancerous cells are different from normal cells to create less toxic and more effective treatments.

A Shift in Treatment Strategies

Identifying and understanding the different subtypes of breast cancer has led to specific treatments for different subtypes. Different tumors may require different targeted treatments; Dennis Slamon, MD, PhD, has been saying for a long time that, “In breast cancer, one size does NOT fit all.”

From the 1880s to the 1970s, it was assumed that breast cancer was most effectively treated with a surgical approach. This notion was based on the assumption that breast cancer could not metastasize to a distant organ (like the liver) without going through the regional lymph nodes. Breast tumors were believed to spread in an orderly fashion from breast to lymph nodes to distant parts of the body. If this were true, then the more aggressive the surgery, the better the chance of cure. Thus, the Halstedian Radical Mastectomy, a very disfiguring surgery that removed breast tissue, lymph nodes and muscle, developed by the surgeon Sir William Stewart Halsted, was the treatment of choice. In the 1960s Bernard Fisher, MD, challenged this assumption. He believed that some tumors were biologically so aggressive that they could bypass lymph nodes and metastasize to distant organs via blood vessels within the tumor itself. In these tumors, a more aggressive surgery would not improve the chance of survival as the tumor would have already spread prior to being clinically detected. He challenged the prevailing notion that radical mastectomy was necessary for every case of breast cancer and undertook randomized clinical studies to evaluate whether a modified radical mastectomy and/or a lumpectomy might be just as effective in treating cancer as the more radical disfiguring Halstedian Radical Mastectomy. In the NSABP Trial, he was able to show that a modified mastectomy was just as effective as a radical mastectomy. He went on to show in multiple randomized studies that lumpectomy plus radiation therapy was as effective as modified radical mastectomy for selected patients. These randomized scientific trials led to a revolution in the surgical approach to breast cancer. Since then there have been six prospective randomized clinical trials comparing breast conservation treatment versus mastectomy that have shown equivalent survival rates for mastectomy compared to surgical removal of the tumor with clear surgical margins followed by moderate-dose radiation therapy to eradicate any residual disease.

Bernard Fisher, MD, also believed that some breast tumors were systemic disease because cancer cells could make their way into the blood stream and other organs without going through the lymph nodes. Initially thought of as a heretic, Dr. Fisher eventually became a hero when he began investigating “adjunct chemotherapy” to prevent the spread of breast cancer to other organs.

The history of chemotherapy for breast cancer began in the late 1950s. In 1958, 826 patients participated in a study in which a chemotherapy agent called Thiotepa was given to half the patients prior to surgery while the other half were given a placebo. The outcomes for the two groups were then compared. Patients with all different types of breast cancer (hormone receptor positive or negative, HER2 positive or negative) were accepted into the study. The use of Thiotepa therapy only proved to be beneficial only with women who were pre-menopausal and had more than three positive lymph nodes, although the trial itself was regarded as unconvincing. In the 1960s there was a study in which post-operative chemotherapy was given as “adjuvant” treatment after surgery. In this study the drug, L-Pam, was administered for two years and researchers determined that there was a survival benefit for women less than 49 years old. We now know that younger women typically have the more aggressive subtypes of cancer that tend to derive more benefit from chemotherapy. Ultimately Dr. Fischer persevered and demonstrated that adjuvant (post-operative) chemotherapy improves disease free survival and overall survival for patients diagnosed with non-metastatic breast cancer.

In the 1970s, oncologists began prescribing multi-agent adjuvant chemotherapy to patients, with the two most common regimens being cyclophosphamide, methotrexate, and 5-fluorouracil (CMF) and Adriamycin/doxorubicin and cyclophosphamide (AC). AC, generally known as doxorubicin, is an anthracycline antibiotic first isolated from the fungus streptomyces peucetius in the early 1960s that works primarily by binding and inhibiting topoisomerase II, a key enzyme in the replication of DNA. Adriamycin was approved for use as an anti-cancer treatment in the United States; AC was adopted as the most common treatment for breast cancer even though CMF and AC were shown to be equivalent in a number of trials. Some scientists suggested that this was because AC was given over a shorter interval—4 cycles compared to 6 of CMF.

In the 1990s the taxanes, such as paclitaxel and docetaxel, were introduced and found to be beneficial in breast cancer treatment. However, no trial tested if taxanes could replace anthracyclines. All trials added taxanes to the anthracycline-based regimens. Oncologists have experimented with different regimens such as changing the order of the drugs or the timing and amount of the drug in different combinations (AC-T, dose dense AC-T and TAC).

The Anthracyline Controversy

When patients with HER2-positive breast cancer were reported to have half the survival time of those with other forms of breast cancer, scientists began to wonder if HER2+ breast cancer had a unique resistance or sensitivity to chemotherapy. All previous studies of chemotherapy had enrolled all types of breast cancer (HER2+ and HER2-). Fortunately, the studies also maintained tissue blocks from the original tumors. A tissue block is the original tissue sample preserved in a block, then sliced very thin for examination after staining. This allowed scientists to go back and test for HER2 in tumors from patients who had previously participated. They then looked to see if HER2+ tumors benefited more or less from anthracycline-based therapies than HER2- tumors. These analyses showed that HER2+ breast cancer tended to have a greater benefit from the use of taxanes compared to HER2-negative tumors. HER2 positive breast cancer seemed to be uniquely sensitive to anthracyclines while HER2- breast cancer did not appear to benefit from anthracyclines. The question then became why? As scientists began genetically mapping the HER2+ tumors they discovered that the gene for HER2 was near the Topo IIa region on the gene. Remember, anthracyclines work by binding to and inhibiting topoisomerase II, a key enzyme involved in DNA synthesis.

In the last 10 years, retrospective analysis of multiple trials comparing anthracycline-based chemotherapy to non-anthracycline-based chemotherapy in breast cancer have failed to show any additive benefit of anthracyclines for HER2-negative breast cancer. There has been no prospective study that has shown any benefit to adding anthracyclines to a taxane-based

**CONTINUED ON PAGE 7**

**EVOLVING INSIGHTS INTO THE RATIONAL TREATMENT OF BREAST CANCER 2011**

**SARA A. HURVITZ, MD, ASSISTANT CLINICAL PROFESSOR OF MEDICINE, DIRECTOR, BREAST CANCER PROGRAM, DEPARTMENT OF MEDICINE DIVISION OF HEMATOLOGY-ONCOLOGY DAVID GEFFEN SCHOOL OF MEDICINE AT UCLA**

This is a summary of a lecture presented on May 10, 2011.
regimen in HER2-negative breast cancer. The role of aromatase inhibitors in HER2-negative breast cancer is thus being called into question by many scientists.

Exposing women (who are potentially already cured by surgery) to toxic treatments that do not improve survival is a serious concern that needs to be addressed by oncologists and scientists. Anthracyclines carry a risk of cardiac toxicity associated with their use. Combinations of trastuzumab, aromatase inhibitors and cyclophosphamide have induced heart failure in as much as 16% of breast cancer patients. Cardiotoxic effects may manifest during early, late or post-treatment; however, early toxicity is uncommon. Chronic, potentially irreversible doxorubicin-associate-ed myopathy (muscle disease) is also a great concern. The damage starts with the first administration, but is seldom noted at low cumulative doses because of cardiac reserves. Some of the factors that are known to increase the incidence of cardiotoxicity include pre-existing cardiac disease, older age, and prior cardiotoxic therapy and radiation to the chest, especially if it is on the left side.

Data examined from the SEER and Medicare database, which includes 31,748 women with stage I to III breast cancer who received chemotherapy versus those that did not, showed that patients who received anthracycline drugs (doxorubicin/adriamycin) had a greater risk of developing congestive heart failure (CHF). Long term data from the NCIC-CTG MA-5 trial which compared CMF to CEF (cytocphosphamide, epirubicin [an anthracycline used instead of Adriamycin/Adriamycin] and 5-fluorouracil) showed a reduction in heart capacity as measured by the left ventricle ejection fraction which was less than 50% at five years for 17% of patients who received CEF, compared to only 2% who received CMF.

A recent study reviewing AC vs. TC found a better disease free survival and overall survival in the TC arm of the study, suggesting that the anthracyclines may not be necessary. There are no studies that have directly answered whether TC is as effective as TAC, but there is one study currently underway for which we are eagerly awaiting results.

Based on all this data, some breast oncologists are now questioning whether anthracyclines are necessary for successful breast cancer treatment. They are very concerned that these toxic side effects can negatively impact the length and quality of life of survivors. Oncologists must now decide how they will treat patients with this current knowledge. Many oncolgists are not yet ready to give up the use of anthracyclines but some academicians, including some at UCLA, believe evidence from a number of trials supports reevaluating standard practices.

Targeted Therapies
The goal of targeted therapies is to specifically target and kill tumor cells while leaving normal cells alone. In order to do this, scientists must have an understanding of the underlying biological reasons that cells become malignant, thus allowing sub-categorization of tumors based on molecular abnormality. In addition, scientists have to know the details about how cancerous cells differ from normal cells so they can develop treatment strategies that directly target these abnormalities. The goal of targeted therapies is to develop therapies that are less toxic yet more effective, while providing more individualized approaches to treatment based on the vast differences in molecular structure of breast cancer. There are ongoing, potential trials working toward developing these treatments.

Estrogen Receptor Positive Breast Cancer
The first targeted treatments involved treatments that blocked estrogen receptors on cancer cells. Tamoxifen interferes with the function of these mutated receptors, following by the development of aromatase inhibitors. Patients with estrogen positive (ER+) and progesterone positive (PR+) stage IV tumors have a 50-75% response rate to endocrine therapies. For patients who are ER+ and PR+, the response rate drops to 30-50%, 20-30% with ER+ and PR- tumors, and less than 10% for patients who are ER- and PR-. There is a substantial advantage in taking tamoxifen for five years for ER+ non-metastatic (stage I-II) breast tumors. For those that do, there is a reduction in 11.8% decrease in the likelihood of a recurrence and a 9.2% reduction in mortality.

One of the questions that has recently been addressed in breast cancer research is whether there is a benefit to adding a Gnordropotin-release hormone (GnRf), which suppresses the production of estrogen in the ovaries of premenopausal women. In Europe, this has been accomplished by giving women an injection of a drug called goserelin. A study has been conducted looking at a control group and treatment arms, in which women received tamoxifen only, goserelin and tamoxifen and goserelin alone to evaluate whether with more suppression is better than one. Women who received nothing had the poorest outcomes; however, women who received both did not have better outcomes than the women who got either tamoxifen alone or goserelin.

In the 1990s, scientists began testing aromatase inhibitors as another form of endocrine therapy for women with ER+ breast cancer. These drugs include anastrozole (arimidex), letrozole (Femara), and exemestane (Aromasin). These endocrine therapies are only for post-menopausal women with ER+ and/or PR+ tumors as they only block production of estrogen from the aromatase enzyme and do not block ovarian production of estrogen. Multiple large randomized clinical trials were performed comparing tamoxifen to an aromatase inhibitor for non-metastatic, ER+ breast cancer in post menopausal women; all of which indicated an additional 2-6% reduction in the risk of breast cancer recurrence compared to tamoxifen for this particular group of women.

In 2010 a study looked at outcomes for two aromatase inhibitors, exemestane versus anastrozole in postmenopausal women with hormone receptor positive primary breast cancer. There were no differences in event free survival or secondary endpoints that included overall survival, distant disease-free survival and disease-specific survival. An updated safety analysis from the BIG 1-98 Trial looked at aromatase inhibitors vs. tamoxifen and found more adverse cardiac events with letrozole while there was an increase of blood clots (thromboembolic events) with tamoxifen. Patients taking tamoxifen have a greater likelihood of developing uterine cancer while all aromatase inhibitors increase fracture risk. When deciding whether to use aromatase inhibitors or tamoxifen, each patient and patient will have to weigh the risks versus benefits of each treatment, taking into consideration the patient’s individual medical history. Tamoxifen has a lower osteoporosis risk in post-menopausal women, decreased frequency of musculoskeletal syndromes and reduced costs, whereas aromatase inhibitors have a reduced risk for deep vein thrombosis, stroke, endometrial cancer and hot flashes. Both have similar effects on neurocognitive status, sexual function, hyperlipidemia and cardiovascular disease.

Since all aromatase inhibitors increase fracture risk, the use of bisphosphonates for the prevention of bone loss has become an important part of the protocol to protect the bones. In a recent trial, ABCSG-22, looked at two different kinds of endocrine therapy (1) tamoxifen plus ovarian suppression and (2) anastrozole plus ovarian suppression, and compared each of these with zoledronic acid added to the regimen. In the first efficacy analysis, there was a 25% reduction in the relative risk of breast cancer recurrence in the patients who received the zoledronic acid with their endocrine therapy. In another study in which letrozole was combined with zoledronic acid given either immediately or delayed in post-menopausal women with hormone receptor positive breast cancer, a 40% reduction in the relative risk of disease recurrence was seen at five years in the women who received immediate zoledronic acid. However, in a larger trial of 3,360 women (The AZURE Trial) zole- dronic Acid (Zometa) was given to women with stage III/IV breast cancer as part of their standard adjuvant treatment. This trial accepted all women, pre- and post-menopausal, and used disease free survival as their primary endpoint. No difference was found in disease free survival for these women who received the bone strengthening medication. However, when a re-analysis was done separating the pre- and post-menopausal women, there was a significant improvement in disease free survival for women who had been postmenopausal for five years and who received zoledronic acid. Another bone strengthener called Denosumab is being evaluated. There is currently an ongoing study to evaluate if it reduces the risk of recurrence.

One of the most important issues to consider for patients who receive zoledronic acid, denosumab or other bisphosphonates is that they need to have good renal function. Also, a small number of patients have a rare adverse effect and develop osteonecrosis of the jaw, a condition which involves exposed bone in the jaw that does not heal easily. Zoledronic acid has a half life of 10 years. Prior to going on this treatment, the oncologist should make sure that patients have seen a dentist and have good oral health. Any needed dental work should be completed prior to this treatment and caution should be taken when dental work should be completed prior to this treatment. They are very concerned that these toxic side effects can negatively impact the length and quality of life of survivors. Oncologists must now decide how they will treat patients with this current knowledge. Many oncologists are not yet ready to give up the use of anthracyclines but some academicians, including some at UCLA, believe evidence from a number of trials supports reevaluating standard practices.
There are approximately 70,000 new cases of bladder cancer per year across the United States. Some states have higher concentrations than others, indicating regional differences that are not well understood. About 20% of all new cases occur in California. In addition to regional differences, gender and ethnicity also play a role; males are twice as likely as females to develop bladder cancer and approximately twice as many non-Hispanic Caucasians, develop bladder cancer than African-Americans, Asian/Pacific Islanders or Hispanics.

There are many things that increase the risk of developing bladder cancer:

- Smoking increases the risk of bladder cancer and smokers have a 2-3 times greater risk compared to non-smokers. While the risk decreases substantially when smoking ceases, the risk remains higher than that of non-smokers.
- The risk increases with age; it is most common in those 60-80 years of age.
- Individuals who work in professions that have contact with chemicals have an increased risk, e.g., contact with rubber, certain dyes, textiles, paint, and hairdressing supplies. Exposure to formaldehyde, a common ingredient used in many products including some of the "Brazilian Blow-outs" to straighten hair, has been implicated in bladder cancer.
- Having a family history of bladder cancer results in an increased risk.

The bladder is only one part of the urinary tract system. It is also made up of the kidney, ureters that carry the urine to the bladder, the sphincter that controls the flow of urine out of the bladder and the urethra which is the tube that carries the urine out of the body. The bladder has two purposes, one is to store urine and the other is to empty itself. The picture below illustrates these body parts.

Bladder Cancer Symptoms and Diagnosis

Many people who are diagnosed with bladder cancer do not experience any symptoms. Some of the symptoms most frequently associated with bladder cancer are blood in the urine (hematuria) and irritative symptoms when urinating (increased frequency of need to urinate, an urgency to urinate quickly and pain during urination). The problem with these symptoms is that they are nonspecific and can apply to other conditions as well. However, they should not be ignored and need to be worked up to find the cause. Most people tend to go to the doctor when they have a lot of blood in their urine, referred to as "gross blood," but men tend to ignore this problem if there is only a little blood in their urine. Sometimes the blood is not visible to the human eye but can be detected through urinalysis.

Bladder cancer is most often diagnosed by a urologist and involves three types of tests. The first test is an x-ray called a CT Urogram where the patient is injected with a small amount of iodine and a series of pictures are made with a CT scanner to image the bladder. The second test is a cystoscopy which uses a small fiberoptic flexible tube that is fed up through the urethra and into the bladder to allow the urologist to see the inside lining of the bladder. This test is slightly easier on women because the urethra is shorter but it can be done as an outpatient on both men and women. Occasionally a rigid scope must be used for treatment purposes but patients are usually sedated for this procedure. The third method is a urine cytology test in which the urine is spun down, put on a microscope slide and the cells are reviewed for abnormalities.

There are different types of tumors characterized by how they look. Froundal tumors look like a bush. Carcinoma in Situ or CIS appears more as a red splotch on the inside of the lining of the bladder. This can be one of the more aggressive forms.

Treatment of Bladder Cancer

Once the diagnosis is confirmed a treatment approach can be determined. Part of the diagnostic work-up includes evaluation to determine whether there is metastatic disease (bladder cancer that has spread outside of the bladder). Most often, the tumor is resected (surgically removed) but depending on the stage of the tumor, the resection may be more involved and there may be other treatments. The old fashioned staging categorized tumors as Stage I, II, III or IV based on how deeply the tumor had invaded the tissue, the grade or how aggressive the tumor cells look on the microscopic view or whether the tumor had spread to other organs. The newer approach looks at the degree to which the tumor (T) has invaded the wall of the bladder, the number of lymph nodes (N) and whether there is metastatic disease (M) and theumbering system is based on these three criteria. Bladder cancer can be resected in two ways. With small tumors that are confined to the bladder, the patient is taken to the operating room, given an anesthetic and a rigid scope that has a cautery loop on it is passed through the urethra into the bladder. The loop is able to heat up and separate the tumor from the bladder. If the tumor is larger, a "neobladder" is constructed and the entire bladder must be removed surgically. This procedure is called a cystectomy, in addition to the bladder, women have their uterus, ovaries and fallopian tubes removed while men have their prostate removed.

The surgeon will then use one of two methods to reconstruct a urinary diversion and create an alternative way to evacuate urine from the body: an ileal conduit or a neobladder. In the ileal conduit the ureters, which are the tubes that carry the urine from the kidneys, are connected by a "loop" of ileum (small intestine) that is brought out to the skin forming a hole called a stoma. It is placed in the lower quadrant of the body and then a removable bag is glued on to this opening. The urine is continuously collected in this bag which has a valve on it and the patient can open the valve into a toilet to empty the bag at regular intervals. The bag is called a "ureostomy bag; patients become very competent and adept at managing this very quickly with the help of an ostomy nurse who guides them in the beginning. This type of surgery has the least amount of complications and is the easiest from which to recover. The downside is, of course, having an external bag that must be worn at all times. The other choice is to create a "neobladder" or new bladder. The neobladder is made by the surgeon from a piece of the small or large intestine. The ureters are diverted into this new bladder and the patient can urinate through their urethra. One of the problems with the neobladder is that it does not automatically contract to empty the way that the natural bladder does. Because it is great for storing urine, but not as great for emptying, it can overfill which creates urinary incontinence. Individuals have to learn to use other muscles to pressure the bladder into emptying. Sometimes patients have to learn to catheterize themselves in order to remove the urine.

Patients that have their tumors resected from the bladder, leaving the bladder intact, may need to have chemotherapy given directly into the bladder. For patients with non-muscle invasive bladder cancer chemotherapy is given when the tumor is high grade, there are multiple tumors or there are recurrent tumors. Patients who have CIS receive bladder chemotherapy. The first line of treatment is BCG (Bacillus Calmette-Guérin), a live attenuated form of Mycobacterium bovis, that is the most commonly used and most successful agent for intravesical therapy. Although the exact mechanism of its antitumor action is unknown, intravesical instillation of BCG triggers a variety of local immune responses which appear to correlate with antitumor activity. Hence it is considered an immunotherapy.

For patients who cannot tolerate the removal of the bladder, radiation therapy is sometimes used.

Patients with muscle-invasive bladder cancer may need chemotherapy given by a medical oncologist. This type of bladder cancer can be life threatening, therefore all
The diagram below illustrates the most common pathways for treating non-metastatic bladder cancer.

**TREATMENT**

<table>
<thead>
<tr>
<th>Non-muscle-invasive</th>
<th>Muscle-invasive</th>
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<tbody>
<tr>
<td><strong>Bladder chemotherapy if:</strong></td>
<td><strong>Bladder removal or Chemo / Radiation</strong></td>
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<tr>
<td>- High-grade</td>
<td></td>
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<tr>
<td>- Multiple tumors</td>
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<td>- Recurrent tumor</td>
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<td><strong>CIS</strong></td>
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<tr>
<td><strong>Bladder chemotherapy:</strong></td>
<td></td>
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<tr>
<td>- BCG, Mitomycin, Others</td>
<td></td>
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<tr>
<td><strong>Regular cystoscopy and kidney x-rays</strong></td>
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**Diagnosis (non-metastatic)**

- **Non-muscle-invasive**
  - Bladder chemotherapy if:
    - High-grade
    - Multiple tumors
    - Recurrent tumor
- **Muscle-invasive**
  - Bladder removal or Chemotherapy / Radiation

**Treatment modalities may come into play. Additional treatments to surgery are needed when the disease has progressed to the lymph nodes or metastasized to other organs. Sometimes a combination of radiation and chemotherapy is given when a patient is not a good candidate for surgery. Surgery is often given before surgery to increase cure rate and survival. It also increases cure rate/survival when given after radical surgery, radiation treatment and increases survival and improves symptoms for patients with metastatic disease. There has been limited research in bladder cancer; however, there was one really good study in which patients received MVAC chemotherapy for 3 months followed by surgery versus immediate surgery alone. There are a variety of chemotherapy combinations that are used and evidence is abstracted from some of the other cancers. Typical drugs include cisplatin, carboplatin, taxanes, 5 – Flol, mitomycin C, gemcitabine. This study showed that chemotherapy alone is not as good as surgery or radiation first.

When the disease is advanced, the prognosis for long term survival is low. The median survival rate is 6-9 months, but treatment can help improve survival time and control disease symptoms such as pain and bleeding.

Patients who have had bladder cancer need to be regularly screened by an urologist as they may develop cancers anywhere along the urothelium, which includes renal/kidney, pelvis, ureter and urethra. Because bladder disease is very chemo-sensitive, it does respond and probably increases survival by a year or two. There are rare cures, probably less than 10%, using the most aggressive chemotherapy. The most aggressive regimens include cisplatin; however, cisplatin-based regimens make people more sick (nausea, fatigue, low blood counts, neuropathy and possible kidney damage) and is not safe for everyone. Individuals receiving cisplatin need excellent kidney function in order to be put on this drug. It tends to be better for younger people who have both kidneys, good kidney function and do not have other confounding medical problems like diabetes, heart or lung diseases, etc.

There are a variety of chemotherapy combinations that are used: methotrexate, vinblintin, adriamycin, and cisplatin (MVAC); gemcitabine and cisplatin (GC); gemcitabine and carboplatin (GCb), Carboplatin and paclitaxel as well as other combinations such as cisplatin, methotrexate and vinblastine (CMV) and cisplatin, cytoxan and adriamycin (CISCA). Single agent chemotherapies such as ifosfamide, pemetrexed, and docetaxel are also used. Chemotherapy has a myriad of side effects such as fatigue, low blood counts, loss of appetite, nausea or vomiting, nerve damage (neuropathy), hair loss, mouth sores, diarrhea, abdominal distress, rash, and irritation of the urinary tract lining leading to bleeding and urgency. A few side effects are okay and can be managed, but many side effects become problematic. It is important that the medical oncologist work hard to mitigate these side effects as much as possible by using a variety of supportive care techniques. Growth factor support such as Neulasta, Neupogen, Procrit, Aromet, and Epogen can be given to stimulate and improve blood counts. To control nausea and vomiting, 5HT3 antagonists (Zofan, Kytril, Anzamet, Aloxi), aprepitant (Emend), prochlorperazine (Compazine) and metoclopramide (Reglan) are given. Sometimes antiemetic medicines are needed and the ones typically given are dexamethasone, prednisone, hydrocortisone, and medrol. Dianexia is managed with loperamide (Imodium), diphenoxylate/atropine (Lomotil) and trinitrate of opium. Pain is controlled through the use of medically prescribed narcotics and gabapentin (Neurontin is often used). If the patient loses his/her appetite, stimulants such as megestrol acetate (Megaace) dronabinol (Marinol) and medical marijuana are used. The anabolic steroid oxandolone (Oxandrin) can help patients who need to gain weight. Uroprotektive medicine (e.g., Mesna) is sometimes given to keep the bladder from bleeding caused by some of the chemotherapies. While some patients may react to the sheer number of drugs, these drugs also allow the patient to more comfortably and safely take the chemotherapy treatments. Strategic use of these supportive medicines can make chemotherapy very tolerable for patients.

Finally, it should be noted that there are some research studies being done that may begin to shed light on bladder cancer and offer other treatment options. Some of these are targeted approaches as well as molecular analysis of tumors.

**Need for Advocacy**

Bladder cancer has been a neglected disease due to poor public exposure and, thus, receives low levels of funding for research investigating more systemic treatments. The Bladder Cancer Advocacy Network (BCAN.org) initially started as a grassroots effort and was spearheaded by Diane Quale whose husband died of this disease a few years ago. Bladder cancer is a significant problem and it can only be improved through better research.

**FOR PATIENTS:**

**Ethical Wills**

Ethical wills are an age old custom for preserving and passing on your values, beliefs, life lessons, hopes for the future, love, and friendship to your family and community.

**Healing Through Art**

A weekly art therapy group to explore the issues faced by individuals with cancer. No art skill required.

**Living Beyond Limits**

Two weekly support groups, one for only women with recurrent or metastatic disease and one open to all patients with recurrent or metastatic disease.

**Look Good; Feel Better**

A 3-hr program for women, co-sponsored with the American Cancer Society. Participants receive complimentary cosmetics and learn skin care, make-up application & the use of wigs and head-coverings.

**Prostate Cancer Group**

A group for men dealing with prostate cancer.

**Women Together**

A weekly, ongoing support group for women being treated for early stage breast cancer.

**Young Adult**

A group for young adults facing the challenges of coping with life and medical issues.

**FOR PATIENTS AND THEIR FAMILY MEMBERS**

**Acupressure**

A program that teaches helpful protocols and acupressure techniques for yourself and your loved ones.

**Circle of Reflections**

An exploration of spiritual journey that cancer creates for each of us. Each month reflects on a different theme.

**Lung Cancer Group**

A weekly support group for lung cancer patients and their caregivers.

**Meditation: Guided Imagery for Inner Healing**

A group designed to optimize emotional, physical and spiritual well-being through meditation & guided imagery.

**Mindfulness Meditation**

A weekly group to enhance well-being in the present moment.

**QiGong**

A weekly group practicing an ancient Chinese movement for restoring health and prolonging life.

**FOR FAMILY MEMBERS & FRIENDS**

**Husbands (Partners) of Women with Cancer**

An evening group for men who live with women diagnosed with cancer.

**GROUPS FOR EDUCATION AND SUPPORT**

**Integrative Oncology Program:**

The following fee-based groups/assessments are conducted by a physician. These programs help you maintain or restore health and wellness, improve quality of life and live as fully as possible.

**Individual Integrative Medicine Assessment**

Meet one-on-one to formulate a plan to maximize your overall health and wellness, based on an in-depth review of your current lifestyle. Topics covered include nutrition, exercise, herbs & supplements, and alternative medicine treatments. Cost is $350.

**Small Group Workshops**

Dr. Hardy is able to offer workshops to small groups, based on a specific diagnosis or issue, e.g. esophageal cancer, post-treatment menopausal symptoms, etc. Please call Marcia at 310-794-1923 to get information on offering a small group workshop.
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Ellen Weinstro
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ALESSANDRA BOLOGNA
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Valerie Walker
WENDY COHEN
Eileen Manuell
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Josie Stewart
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Grace Middendorf
Harvey Sitzer
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Helen Wong
SUSAN ZAGER
David Zager

In Honor of:

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John Auto
KAUSER AHMED
Sohn & Siyamou Feigl
Yovette Wanders Peterson
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Colorectal cancer is the second most common cancer in the United States. There are an estimated 145,290 cases and 54,290 deaths per year in the US. It is the second leading cause of cancer death in men and women. Colorectal cancer is a dominant disease in the Western part of the world; there is a greater risk of developing it in both the United States and Western Europe and a lower risk in Asia, Africa, and much of Latin America.

The life time risk of developing colorectal cancer is about 6%, which is second in frequency compared to breast cancer. Ninety percent of the cases of colorectal cancer occur in patients who are over the age of 50, although there are an increasing number of people aged 35-45 who are being diagnosed. The increase in malignancies among younger people is a growing concern.

A lot of research has been done on diet and eating habits and we know that when there is a higher intake of high fat and low fiber foods, there is also an overall increase in colon cancer. Many studies have looked at the eating patterns of immigrant populations with a low frequency of colon cancer and determined that people who migrate to areas in which the colon cancer rates are higher show an increase in colon cancer within 1-2 generations in their new environment. Many scientists feel diet plays a big role and find the Standard American Diet, (SAD), to be seriously lacking in micronutrients and fiber. Fiber, the indigestible component of vegetables, is particularly important. Internationally, there is a correlation between increased dietary fiber (fruits and vegetables) and a reduction in the risk of developing colon cancer. Obesity, physical inactivity and high fat/low-fiber diets increase your risk of colo-rectal cancer.

Like many other cancers, the risk of colon cancer increases as we age. You are at an increased risk if you have a family history of colon cancer (parent, sibling, aunt, uncle or child) with a history of colo-rectal cancer or adenomas, polyps or inflammatory bowel disease (ulcerative colitis and Crohn’s disease). While the majority of people with a family history of colon cancer do not develop cancer, there are two well-described genetic syndromes that give rise to colon cancer. Familial adenomatous polyposis results in the production of many polyps and even cancer at an early age. In Hereditary Nonpolyposis Colorectal Cancer (HNPCC or Lynch Syndrome), family members tend to develop colorectal and sometimes uterine, stomach and/or ovarian cancers. Physicians and genetic counselors play an important role in helping families determine whether or not they are carrying a mutated gene that would put them at higher risk for developing these conditions. Individuals who have ulcerative colitis are also at increased risk. People at high risk should adhere to strict screening guidelines. It appears that environmental factors play a role although the exact nature is not completely clear. Certain drugs, such as hormone therapy and cox-2 inhibitors, seem to reduce the risk of developing colon cancer.

Eating a healthy diet has many benefits and is recommended for overall anti-cancer reduction, diabetes prevention and prevention of heart disease. However, even if you have a healthy lifestyle with exercise and eat a healthy diet-rich in fiber, low in fat and high in micronutrients—you must still be regularly screened for colon cancer.

Screening for Colon Cancer

The single most important step that you can take to prevent colon cancer and the risk of mortality from colon cancer is to have regular screenings. While there has been some debate in the medical field about which tests are the best, there is no debate as to whether people should get regular screenings. The gold standard for screening is the colonoscopy, which allows visualization of the entire colon.

The most effective methods of screening and early detection involve cleaning out the colon and allowing a trained physician to look at the interior walls. This procedure is actually very well tolerated, the reasons behind it are important, and everyone should follow the screening guidelines. The U.S. guidelines as followed by the American Cancer Society: Guidelines for mammograms, pap smears and teeth cleanings. Screening allows physicians to catch early stage colon cancer, which ultimately reduces mortality. The bottom line is that the death rate from colon cancer would drop by at least two-thirds if everyone who should be screened had regular screenings. In reality, only 30-40% of eligible adults are ever screened for colon cancer. While the death rate is going down because more people are getting screened, there are still improvements to be made. What are the common screenings?

Fecal occult blood testing: This is one of the oldest tests to show a reduction in mortality. With this test, the patient or his/her physician smears a small amount of feces on a card treated to detect the presence of blood in stools. This test is inexpensive and easy for the patient to perform. It is not as sensitive as an endoscopy (see below) to the presence of cancer because it detects only the presence of blood. If a tumor is not bleeding, it will not be detected. Furthermore, other conditions can cause bleeding, so additional screening and follow-up become necessary if the test is positive. Three studies, however, showed a reduction in mortality up to 33% when this basic test was used as a screening tool.

Flexible Sigmoidoscopy: This procedure uses a flexible instrument that has a video camera, irrigation capabilities and the ability to take biopsies while viewing the colon. It can see about 24 inches of the colon starting at the rectum which is the lowest 1/3 of the colon. It takes approximately five to 10 minutes and can be done by primary care physicians and nurses. Patients sometimes experience an uncomfortable bloated feeling as air must be used to inflate the colon to make it visible. Patients must have two enemas prior to this procedure to clean out the portion of the colon that will be viewed. This method screens only one portion of the colon, although it is the portion in which more than 50% of polyps and cancers are usually detected.

Colonoscopy: This procedure is the most accurate way to examine the colon because it allows your physician to see the entire colon. The patient is usually sedated and the procedure is performed as an outpatient. If polyps are detected during the colonoscopy, they can usually be removed at the same time, helping to prevent cancer. Colonoscopies require the colon to be completely cleaned out so that the lining is clean and visible through the scope, allowing the physician to detect any abnormalities. It requires more prep but is 95% accurate.

Virtual Colonoscopy (CT colography): This technique utilizes high resolution helical CT scanning to create two-dimensional and three-dimensional images. The virtual colonoscopy still requires a complete clean-out procedure in order to image the colon and the insertion of air to inflate the colon for contrast in the image. It does not allow the physician to biopsy a polyp at the time of the procedure and, thus, may require a second clean out and a follow-up colonoscopy if something is seen. It appears to be as good as a colonoscopy for detecting lesions greater than 1 cm, but may not detect smaller lesions. This may be a good option for patients who cannot undergo a colonoscopy and might also eliminate a large number of people who really don’t need a colonoscopy for having a CT scan. We need to see more studies on this procedure and may ultimately be less expensive.

In the future, prevention of colon cancer may include recommendations such as calcium and cox-2 inhibitors. There is no good medical reason to believe that these procedures are necessary or even helpful. The virtual colonoscopy still requires a complete clean-out procedure in order to image the colon and the rectum. The virtual colonoscopy is now an important tool for patients who cannot undergo a colonoscopy and might be used for patients who really don’t need a colonoscopy for having a colonoscopy every year. These issues should be discussed with your primary doctor. If you have a family history, it is important to meet with a gastroenterologist to establish an appropriate screening pattern. If you have a family that was diagnosed with colon cancer before the age of 50, your screenings need to be done on a more regular basis and should start approximately 10 years before the date of your first diagnosis. So, for example, if your mother was diagnosed with colon cancer at 40, you should have your first colonoscopy at age 30!

Biology of Colon Cancer

To understand colorectal cancers, it helps to understand the anatomy of the colon and the rectum. The colon is shaped like a big question mark. It is made up of the cecum, the ascending colon, the transverse colon, the descending colon, the sigmoid colon (which curves around like the Greek letter sigma) and finally the rectum which is where the stool is stored until you are ready to have a bowel movement. Cancer can occur along any part of the colon although some areas are more likely than others to develop cancers. Approximately half of all colon cancers occur in the sigmoid colon and rectum. Despite some hype that suggests that cancers are encrusted and need to be cleaned out periodically by colonics and enemas, there is no good medical reason to believe that these procedures are necessary or even helpful. The colon is pink and soft and quite smooth.

The development of colo-rectal cancer is a multifactorial process involving sequential genetic changes. Specific gene mutations correlate with distinct histopathologic changes. Progression from normal mucosa to carcinoma involves a series of mutations affecting multiple genes that regulate growth, differentiation of cells and normal cell death (apoptosis). Most colon cancers develop from glandular benign tumors called adenocen -
Colorectal cancers develop from adenomatous polyps, but most adenomatous polyps do not become colorectal cancers. Approximately 50% of us will develop a polyp in our life but 90% of these will not be cancer. Patients who develop adenomatous polyps have an increased risk for developing colon cancer; the larger the polyp, the greater the risk of developing cancer. It takes a long time for these polyps to turn into cancer, which provides an opportunity, through screening, to detect and treat them before they develop into cancer.

People with a personal history of polyps have a 1½–2 times higher risk of developing colorectal cancer depending on the number, size and histology of the polyp. People with a personal history of colon cancer have a 1½–2 times greater risk of developing another colon cancer. Individuals with inflammatory bowel disease such as Crohn’s and ulcerative colitis are also at an increased risk. Family risk includes having first degree relatives such as parents, siblings, aunts, uncles and children and requires increased attention to screening.

Colon cancers have genetic changes but only a small number can be attributed to a particular gene. Some mutations have been identified, such as K-Ras, APC, DCC, P53 (85%) and DNA and MRR (15%). Some people also carry genetic mutations that exist within DCC, P53 (85%) and DNA and MRR (15%). Some mutations have been identified, such as K-Ras, APC, DCC, P53 (85%) and DNA and MRR (15%). Some mutations have been identified, such as K-Ras, APC, DCC, P53 (85%) and DNA and MRR (15%). Some mutations have been identified, such as K-Ras, APC, DCC, P53 (85%) and DNA and MRR (15%). Some mutations have been identified, such as K-Ras, APC, DCC, P53 (85%) and DNA and MRR (15%). Some mutations have been identified, such as K-Ras, APC, DCC, P53 (85%) and DNA and MRR (15%).

Biological therapies are used in advanced disease. In particular, angiogenesis inhibitors have been very important. In order for cancers to continue to grow, they need to correlate tumor biology with outcomes. The goal of changing how cancer is treated. With all of these efforts, we look forward to changing how colon cancer is treated over the next 10–15 years.

In summary, colon and rectal cancers are best treated with a multidisciplinary approach. Proper staging and surgery is essential for the best results. Some patients with metastatic disease can now be cured. There is a need to correlate tumor biology with outcomes. The future is in molecular testing of tumors, gene arrays, new targets, and new drugs aimed at those targets. UCLA is committed to this research-based approach to the clinic, advancing treatment of cancer throughout the continuum.
States from the southern portion, which is about 40%.

During the winter. This parallel cuts across the United States separating the northern portion of the United Kingdom is insufficient. A study published in 2001 found that postmenopausal women were significantly VD deficient. A 2005 study determined that approximately 97% of the population has less than 80 nmol/L, which would be the equivalent of a 45ng/ml on the blood test used in the US. Sixty-one percent have less than 50 nmol/L and 34% have less than 40 nmol/L.

Certain populations are at an increased risk of being VD deficient. The elderly, home bound and critically ill patients as well as people who are obese, pregnant, children and adults spend more time in the sun and are at increased risk of skin cancer prevention; more people are staying out of the sun and using sunscreen, contributing to decreased VD levels. As sunscreen blocks UV radiation from the sun, it also interferes with the body’s ability to use that energy to activate VD in the skin. People with darker complexion are at even greater risk because they have more melanin in their skin, which protects them from the sun but also inhibits their ability to absorb the ultraviolet rays needed for making VD.

Some have questioned why we now have this problem; it may have a lot to do with the changing nature of the way we live. Children and adults spend less time outdoors in their work activities and at play. Children spend more time inside on electronic devices playing games and adults work indoors rather than outside. There is an overall reduction in the amount of time that people of all ages spend in the sun. In addition, there is an increase in the use of sunscreens, as we have become more concerned about skin cancer prevention.

There is also a decrease in the consumption of VD rich foods and a greater ethnic diversity in the US population. There is a clear correlation between where you live and the latitude in which you live. People who live above the 27th parallel have very little VD production occurring in their skin during the winter. This parallel cuts across the United States separating the northern portion of the United States from the southern portion, which is about 40% of the US falling below the 27th parallel.

In summary, the risk factors for VD deficiency include being over the age of 65, having dark skin, insufficient sunlight exposure (due to being house bound and in the northern latitude during winter), certain medications (e.g., anticonvulsant and glucocorticoid steroids), obesity, a sedentary lifestyle, chronic kidney disease, liver failure, and malabsorption caused by a disease that affects how your body absorbs vitamins. For example, patients with Crohn’s disease, cystic fibrosis, sarcoid disease, liver disease or people who have had a Whipple procedure have difficulties absorbing VD.

For the most part, much of the known information about the benefits of VD has been focused on bone health, although more recent research has found associations between lower levels of VD and other problems such as infections, some mental disorders such as schizophrenia and depression, asthma and other lung conditions, high blood pressure, coronary heart disease, autoimmune diseases, psoriasis, diabetes Type 1 and 2, obesity, type 2 diabetes, multiple sclerosis, and aches, osteoarthritis, osteoporosis, bone pain, rickets and certain types of cancer — breast, colon, prostate, pancreas etc. When looking at studies reporting all-cause mortality (rate of death from all causes), Vitamin D seems to be protective; there are lower mortality rates in populations with higher levels of VD.

Many mechanisms have been proposed to explain the beneficial effect of Vitamin D on cancer. Vitamin D has a healthy effect on the immune system and helps improve cell differentiation, natural cell death (apoptosis), and is associated with the inhibition of cells’ ability to create new blood vessel growth. All of these associations suggest that VD at sufficient levels may be a factor in the ability to protect oneself from cancer. In a 2010 study looking at VD levels in newly diagnosed breast cancer patients, three quarters of the patients had low or insufficient levels of VD. In additional studies, it has been shown that 800 IU’s of VD is not enough to increase the levels even when supplemented with 16,000 IU’s for two weeks in this breast cancer population.

A 2006 study that looked at 25-hydroxy-vitamin D3 (the molecule that is measured through blood tests) levels found no correlation with cancer of the brain, melanoma, or multiple myeloma; however, there was association with bladder, lung, advanced prostate cancer, non-Hodgkin lymphomas, kidney, colorectal, stomach, pancreas, leukemia, esophagus, and oral cancers. Some research suggests that VD levels over 30ng/ml, (the metric standard) have a protective effect against the development of cancers.

A randomized controlled trial was done in which people were assigned to one of three regimens (1) either placebo of both vitamin D and calcium, (2) calcium only or (3) calcium and vitamin D for four years. Of the 1180 patients who were randomized, 1024 completed the four-year study, which is a high completion rate. The cancer incidence and rate was a main secondary outcome of the study. All patients in the placebo group had the highest risk of developing cancers while the group that received calcium and VD had the lowest risk. There was an 80% protective effect determined for those participants who had the highest levels of VD. In another study, the relative risk of colon cancer decreased with Vitamin D as did the risk of getting fractures, while the amount of time able to walk and overall muscle strength went up for patients with higher levels of VD. Vitamin D also seems to have quality of life implications. Patients who receive aromatase inhibitors who have 40–50ng (nanograms) of VD, as measured in their blood, had fewer bone and joint pain side effects. Having fewer negative side effects increases the patient’s probability that he/she will continue treatment and be able to take these life-saving medications.

How Much Vitamin D and How Best to Get It?

Two of the questions that arise with any vitamin are (1) what is the best way to get it and (2) how much should you take? With Vitamin D, risk/benefit assessment needs to be done and should be tailored to you taking into account your individual goals, risk factors, dietary habits, and other health conditions. First look to diet to increase intake. The best sources of VD are dairy products that are VD fortified, deep water fish such as cod and sardines and vitamin supplementation. Dietary sources alone, even combined with some judicious sun exposure, is usually not enough to raise your VD to optimal levels. Supplementation is usually necessary. However, it is important to find out what your starting VD level is before you begin supplementation. Your primary physician can and should test for your VD level as part of your annual work-up. When VD is measured from a blood test, the actual molecule that is being measured is called 25-hydroxyvitamin D3. In the United States that level is typically measured in nanograms. Vitamin D levels are considered normal if the blood level is over 35ng/ml but for different medical conditions other levels would be considered optimal. This should be discussed with your provider.

Below is a list of food sources and the amount of VD that can be obtained from each source. This partial list provides an idea of how much VD can be obtained from food:

- Fortified sources
  - Cod liver oil 100 IU per serving
  - Milk 100 IU per 8 oz
  - Orange juice 100 IU per 8 oz

- Non-fortified food sources
  - Breast milk 20 IU per 1 oz
  - Cod liver oil 400 IU per teaspoon
  - Egg yolk 20 IU
  - Mackerel (canned) 250 IU per 3.5 oz
  - Salmon (canned) 300 to 600 IU per 3.5 oz.
  - Salmon (fresh, farmed) 1000 IU per 3.5 oz.
  - Salmon (fresh, wild) 600 to 1000 IU per 3.5 oz.
  - Sardines (canned) 300 IU per 3.5 oz.
  - Tuna (canned) 230 IU per 3.6 oz.

If you are VD deficient, you will need significant supplementation and might be given a prescription by your doctor. This usually involves taking a large amount of Vitamin D2. Recent research has suggested that weekly or daily supplementation is better than the older multiple dose regimen. Most people have quality of life implications. Patients who receive aromatase inhibitors who have 40–50ng (nanograms) of VD, as measured in their blood, had fewer bone and joint pain side effects. Having fewer negative side effects increases the patient’s probability that he/she will continue treatment and be able to take these life-saving medications.
the vitamin so more of it is available for the body to use. It is important to monitor your VD levels and find the best dosage for your maintenance, once you have achieved an appropriate level. In a recent study of elderly veterans that were VD deficient, 2000 IU’s were used for 6 months.

The Institute of Medicine (IOM) recommends that adults between the age of 19 and 70 get 400-800 IU’s (International Units=IU) of VD per day up to 4,000 IU’s. For adults over 70 years of age, they recommend 800 IU’s also up to 4,000 IU’s per day. For many, the 600-800 IU’s seems like a conservative approach. One study suggested that all-cause mortality dips when blood levels are maintained between about 30 and 45ng’s. The IOM is concerned with one study that showed a slight increase in all-cause mortality when the blood levels of VD were in the 50 to 60 range. It is not clear whether this will hold true over time.

There are a few potential adverse effects of VD and calcium. High rates of calcium can increase the likelihood of developing kidney stones by about 14%. If a person already has a high calcium level, taking a lot of VD could cause the calcium level to go higher. This effect however is not observed in all patients. It has not been proven yet that VD actually reduces the risk of recurrence of cancer, but normalizing Vitamin D levels is still recommended based on knowing that there is a lower incidence of cancer in those with adequate VD levels. For patients with melanoma or people at high risk for melanoma, getting VD from the sun is not a good idea because the same wavelength that is necessary for VD production is also the same wavelength that causes melanoma. There are a few other contraindications for VD supplementation. Patients who have granulomatous disease, including TB and sarcoidosis, should consult their physician before supplementing with VD. Patients with metastatic bone disease and individuals with a rare genetic illness called William’s Syndrome should also not supplement their VD. If patients have symptoms of toxicity – kidney stones (nephropathy-calcinosis), plaque in the arteries (vascular calcinosis), inflammation of the pancreas (pancreatitis) and high levels of calcium (hypercalcemia) – then VD supplements need to be stopped and readdressed with their physician.

Recommendations
Know your VD number! Ask your physician to order a Vitamin D blood test as part of your regular laboratory regimen. Once you have your baseline, you should have it checked regularly until it reaches an optimal level and remains stable. It takes about 4-6 weeks to see a change in your blood level after you have made changes in supplementation amounts. Optimize your food sources but be careful when increasing fish to not eat too much fish containing mercury, as this can be problematic for different reasons. You can get information about which fish is safe to eat by going to the Monterey Bay Aquarium Seafood Watch site and downloading their seafood guides: http://www.montereybayaquarium.org/cr/seafoodwatch/download.asp. If it is not contaminated, get approximately 15-20 minutes of sun, exposing legs and arms at the very least. Be judicious in your sun exposure if you have had a cancer or are taking a medication that makes your skin sun sensitive. Always use high quality well-manufactured supplements. Chewable supplements may make some VD available to the body as it begins getting absorbed in the mouth. Whenever using supplements, make sure you have the facts, continue to stay updated, and individualize your plan in a thoughtful evidence-based way with attention to your own individual circumstances and health history.

[Editor’s Note: If you are interested in a more personalized discussion of your vitamin D level, the integrative oncology assessments done in the Simms/Mann – UCLA Center for Integrative Oncology often addresses these issues. In addition, the Reflections Boutique located in the 200 UCLA Medical Plaza, Suite 163 provides high quality supplements including chewable vitamin D. Purchases can be made in the store, by telephone 310 794-9080 or online through the Center distribution Center at www.SimmsMannCenter.ucla.edu]. Note that any revenues generated from Reflections goes to supporting the free psychosocial and educational services offered in the Simms/Mann – UCLA Center for Integrative Oncology.]
SYMPTOM MANAGEMENT DURING CANCER TREATMENT

THOMAS STROUSE, MD, MEDICAL DIRECTOR, UCLLA RESNICK NEUROPSYCHIATRIC HOSPITAL, PROFESSOR OF CLINICAL PSYCHIATRY AND VICE-CHAIR FOR CLINICAL AFFAIRS, DEPARTMENT OF PSYCHIATRY AND BIOBEHAVIORAL SCIENCES, DAVID GEFFEN SCHOOL OF MEDICINE

This is a summary of a lecture presented on September 13, 2011.

In order to effectively discuss symptom management, it is helpful to understand what “symptom” means. Symptoms are the subjective evidence of disease or physical disturbance observed by a patient according to the Webster’s Dictionary. In general, symptoms are not observable by others and they must be described or reported by the individual in order to be understood, assessed and acted upon. It is important for the care team of a patient with cancer to understand the symptoms that are being experienced. Sometimes they may be hard to describe. There is a great body of shared language around symptom description, but it is incumbent upon the patient to report symptoms to their team and to sort through them together.

Common Symptoms During Cancer Treatment

There are a variety of symptoms that are common during cancer treatment and sometimes after as well. Only in the last 20 years have these symptoms been adequately documented, and for some there is still a lot to be investigated and understood. These common symptoms include the following:

- Pain
- Nausea
- Fatigue
- Appetite problems
- Low mood
- Anxiety/lowest
- Breathing discomfort/difficulties/cough
- Fever, sweats, hot flashes
- Constipation
- Diarrhea
- Other gastrointestinal distress: dry mouth, taste changes, etc
- Nighttime sleep problems
- Daytime sleepiness
- Concentration/thinking/memory problems

It is important to understand the cause of the symptom when possible, because the same symptom may result from different sources, changing how the symptom is treated. Some symptoms can originate from the disease itself. For example, a tumor pressing on a nerve can cause pain. Side effects of treatments can also cause symptoms. Sometimes a person has a pre-existing disorder and those symptoms may get better, stay the same or even get worse due to the cancer or the treatment. Symptoms may appear during cancer treatment or subsequent to cancer treatment, and may not be related to the cancer at all. Symptoms may be related to a new non-cancer-related illness, thus it is very important that assumptions are not made about symptoms without first working up the symptoms to better understand them and their root source. There can be other causes as well.

When evaluating symptoms, it is important to look at the sum of the severity of the symptoms to evaluate how significantly they are affecting the quality of a person’s life. This is often referred to as the symptom burden. Sometimes the burden of the symptoms may outweigh the benefits of the treatment and are just too taxing for the individual. It has been important for researchers to understand the symptom burden of treatments and cancers. It is helpful to understand typical patterns and differences among specific kinds of cancers and specific cancer treatments. It also helps to guide studies of optimal management strategies, relieve suffering, and help people complete difficult treatments that are aimed at reducing or ameliorating the cancer. As an example, interferon treatments sometimes come with significant increases in depression. Through research it was learned that pre-treating patients with anti-depressant medications could help them avoid depression, thus reducing the symptom burden.

Many patients are reluctant to report side effects and symptoms to their doctors during treatment. There is no correlation between the number or intensity of treatment-related side effects and the outcome of the treatment. Sometimes patients are in doubt about what to report, but they should report all of their symptoms and allow the physician to help sort out what is most important and how best to treat them. Even if they are not asked about symptoms, patients should report them.

Beginning in the early 1990s, national organizations began to do rigorous scientific reviews of practice patterns for treatments of cancers and symptoms because there were so many regional differences in how treatments were being used. This was done by gathering experts together, having them read all of the published studies, rank their quality, and assess the number of people that participated, considering both the quality and quantity of the data on a particular topic. This resulted in published studies summarizing these reviews, which are periodically updated, and as a result, many “evidence-based” treatment guidelines have become the norm. In 1994 the first set of treatment guidelines for pain was published and has since been revised.

One problem patients face is the amount of information that is available on the web. While there are many very good resources, there is no regulation of health claims that are made by websites or individuals. There are a wide array of compounds and services that can be purchased directly by consumers and there has been an increase in “pseudo-scientific” advertising that looks like journal articles, but are really not scientific. There can be a lot of intentionally misleading information, making it difficult for patients to sort through what is reliable, and because of the impact of cancer on their lives and the high degree of need to reduce that impact, patients and family members may be vulnerable to these unsubstantiated claims. It is important to remember, “Buyer Beware.” There are some good web-based resources for patients and families with cancer and they include the following:

- National Comprehensive Cancer Network (NCCN)
- American Cancer Society patient portal: Cancer.org
- MyAACS
- National Cancer Institute: cancer.gov
- The Cochrane Collaborative

Evidence-based Treatments for Common Symptoms

- Pain

Pain is one of the most common symptoms associated with cancer and cancer treatment and it can occur at any phase of the disease. It is the most studied of all symptoms. It is important to take a focused approach, first try to understand the cause of the pain, as this may determine which treatment is best. There are a variety of issues that can cause pain including surgery, pain from a tumor growing and pressing on nerves and pain from some of the anti-tumor therapies that cause peripheral neuropathy, or muscle and body aches often caused by aromatase inhibitors used in breast cancer. There is a wide array of pain medications that can be useful including opioids (of which there are many different kinds and strengths), non-steroidal anti-inflammation medications (e.g., ibuprofen and Celebrex), and medications for nerve pain that fall in the category of anticonvulsant medications (e.g., gabapentin and Lyrica). There are also many intervention procedures that can be used to treat pain including nerve blocks, and steroids. Behavioral approaches that include cognitive behavior therapy, relaxation, and mindfulness can also be effective. Physical therapy methods or other postural techniques may be useful depending on the source of the pain. Acupuncture is also beneficial, especially in neuropathic (nerve based) pain.

- Nausea

How we treat nausea has changed significantly in the last 10-15 years. There are multiple drug classes that are helpful to patients including: 5HT3 antagonists (ondansetron, granisetron, etc.) - Neurokinin-1 inhibitors (aprepitant, fosaprepitant) - Vanilloid-receptor agonists (nabilone, dronabinol) "Conventional" cannabinoids—drugs that have some of the active ingredient of marijuana but are manufactured to a pharmaceutical standard. While marijuana may have a role, a physician should be consulted and the impact of singeing one’s lungs with hot smoke should be considered as it might be more harmful than helpful.

- Fatigue

Fatigue is a prevalent complaint by patients and one that is very uncomfortable for them to live with. It is also one of the most difficult to treat. Initially it was thought that fatigue could be managed if the hemoglobin was maintained above 10 mg/dl but over time we have come to understand that it is much more complicated than that. There are many different thoughts about the causes of fatigue and for many patients its roots may be multi-factorial. In addition to keeping hemoglobin ranges elevated, there are a variety of treatment approaches that are helpful when used in conjunction with each other to increase the likelihood of altering the fatigue. Self-pacing is an important concept in which individuals learn how to conserve and use their energy on the things that are most important for them. Patients must adjust to the fact that they do not have an endless supply of energy and must learn to allocate it throughout the day with alternating periods of rest. Poor sleep often contributes to fatigue, thus managing pain and other symptoms may help to improve sleep. In addition, there are a group of techniques referred to as “sleep hygiene” in which patients must engage in behaviors to train themselves to get the most sleep available. Sleep hygiene is about using the bed only for sleep, avoiding activitiy just before sleep, potentially darkening the room and keeping it relaxed and quiet, eliminating stimuli such as a computer, cell phone and televisions from the bedroom, not exercis-
It is important to differentiate between night sweats and flashes, which might be a result of the treatment. Night sweats are a symptom of some malignancies, and tend to improve as the malignancy is controlled by treatment. Hot flashes are often hormonally mediated. Menopause or induced menopause from treatment can cause hot flashes. These are typically seen in breast, prostate and ovarian cancer patients. Hot flashes are responsive to two major drug classes, selective serotonin reuptake inhibitors and gabapentin. Rigorous clinical trials of dietary soy, flaxseed and black cohosh in general have been disappointing.

Constipation and Diarrhea

Constipation and diarrhea are symptoms that tend to be trivialized, but can be debilitating, life threatening and should not be ignored. They are often not simple problems and require some careful attention to adequately treat. Constipation may require stool softeners, laxatives, dietary modifications of fruits, vegetables and fiber; physical activity and adequate hydration. Metronidazole is a medication that can be given to block the negative effects of narcotics on the bowel, thus reducing the likelihood of developing constipation from the slowing motility of the bowel, which is a side effect of opioid medications. Diarrhea can lead to dehydration and it is important it be effectively treated. The best treatments include drugs that slow motility, dietary modification and adequate hydration. Seeing someone with expertise in nutrition can be helpful for treating these symptoms and preventing them.

Dry Mouth/Taste Changes

Salivary glands can be affected by chemo-therapy, radiation treatments and surgery. Artificial saliva can be helpful if the salivary glands have been damaged, which happens when they are in the radiation field. Drugs that stimulate saliva production such as pilocarpine and orlistat can be helpful for mouth sores and dry mouth. There is a small body of literature on acupuncture. Someone with expertise in nutrition can be very helpful as well.

Sleep Problems (Insomnia)

There are a large number of people who sleep problems even without a cancer diagnosis; and for those who had pre-existing difficulties, the cancer diagnosis and treatment can make it worse. For those who slept well prior to cancer, sleep can become disrupted after the diagnosis. It is important to minimize activating drugs near bedtime such as caffeine and corticosteroids. “Sleep Hygiene” as noted earlier is an important component of managing sleep disruptions. Treatments that reduce stress and distress, including cognitive behavioral strategies, relaxation and meditation can be helpful. Sedative-hypnotic medications can also be used to facilitate sleep.

Depression and Anxiety

It is important for professionals to distinguish normal reactions from disorders, though normal reactions can also benefit from psychological approaches. Some malignancies such as pancreatic cancer or biliary lesions are highly associated with depression. Anxiety is commonly associated with carcinoid tumors because they produce a lot of serotonin. It is important to have a thorough work-up of these symptoms and, when possible, eliminate treatments or medications that might be causing mood or anxiety based side effects. There is strong evidence for behavioral interventions and psychotherapies, especially those that use cognitive behavioral techniques. A referral to a psychiatrist for medication evaluation is also appropriate, especially one who is trained in the field of oncology and understands the unique needs of the population. Patients should not assume that they need to live with these symptoms which can be debilitating and make coping with a difficult diagnosis more difficult. Anxiety and depression can also stem from untreated symptoms such as pain, thus treating all symptoms is an important goal in caring for someone with mood and anxiety symptoms.

Thinking/Memory Problems

Cognitive changes after cancer and its treatment is an area of interest in which there is ongoing research. It is important to determine if there are new symptoms, or persistent or progressive symptoms that occurred prior to the cancer. If they are of new onset, it is important to scrutinize current treatments for the cause. Benadryl frequently blocks the acetylcholine receptors and can produce significant cognitive impairment. When no obvious source is identified, thinking/memory problems may be seen as non-specific correlates of the disease or treatment that generally improve over time. There is no evidence to suggest that the cognitive enhancers used in the treatment of dementia will be helpful for cancer treatment-related memory problems. Ritalin has been helpful for some people who have difficulty attending, but it does not necessarily make the cognitive dysfunction better.

From Evidence Based to Personal Decision Making

It is essential that patients develop a collaborative working relationship with a local health professional, ideally palliative care were found to have improved quality of life, optimizing quality of life by anticipating, preventing, and treating suffering. Palliative care throughout the continuum of illness involves addressing physical, intellectual, emotional, social, and spiritual needs and to facilitate patient autonomy, access to information, and choice.” The World Health Organization in 2006, penned this description, “an approach that improves the quality of life of patients and their families facing the problems associated with life-threatening illness, through the prevention and relief of suffering by means of early identification and impeccable assessment and treatment of pain and other problems, physical, psycho-social, and spiritual.” Traditionally, palliative care has been broadly applied to those with life threatening or debilitating illness, however, more recently there has been a push to see palliative care as integral to care at any phase of the illness, regardless of expectation for a prompt cure, a long term remission, an uncertain course or a grave and imminent prognosis. A recent study of patients with lung cancer who were diagnosed with advanced disease demonstrated the benefits of early palliative care. Patients on a 12 week trial who received augmented and early palliative care services with the hope that this will yield benefits in early identification and impeccable assessment and treatment of pain and other problems, physical, psycho-social and spiritual.

Palliative Care

In 2008 in the Federal Register as, “...patient and family-centered care that optimizes quality of life by anticipating, preventing, and treating suffering. Palliative care throughout the continuum of illness involves addressing physical, intellectual, emotional, social, and spiritual needs and to facilitate patient autonomy, access to information, and choice.” The World Health Organization in 2006, penned this description, “an approach that improves the quality of life of patients and their families facing the problems associated with life-threatening illness, through the prevention and relief of suffering by means of early identification and impeccable assessment and treatment of pain and other problems, physical, psycho-social, and spiritual.” Traditionally, palliative care has been broadly applied to those with life threatening or debilitating illness, however, more recently there has been a push to see palliative care as integral to care at any phase of the illness, regardless of expectation for a prompt cure, a long term remission, an uncertain course or a grave and imminent prognosis. A recent study of patients with lung cancer who were diagnosed with advanced disease demonstrated the benefits of early palliative care. Patients on a 12 week trial who received augmented and early palliative care services with the hope that this will yield benefits in early identification and impeccable assessment and treatment of pain and other problems, physical, psycho-social and spiritual.
Another target being studied for hormone sensitive breast cancers are treatments called mTOR inhibitors which work at a deeper level, changing the signaling within the cell. A phase II randomized study of tamoxifen with RAD001 (TAMRAD) in hormone positive women with metastatic breast cancer prior to exposure to aromatase inhibitors found a higher incidence of tumor shrinkage in the women treated with both drugs compared to tamoxifen alone. In addition, the amount of time before the progression of the disease also increased. As of October 10, 2011, there has been increased overall survival as well.

HER2 Positive Breast Cancer

In 2001, the pivotal trial of trastuzumab in HER2+ breast cancer showed that patients who were treated with trastuzumab added to chemotherapy was shown to yield a significant improvement in survival and time to progression compared to chemotherapy alone. This study led to the FDA approval of trastuzumab for stage IV HER2+ breast cancer. Since that time over 12,000 women with non-metastatic HER2+ breast cancer have been evaluated in randomized clinical trials (comparing chemotherapy alone or in combination with trastuzumab). These large studies have all indicated that there is a significant improvement in survival and a reduction in recurrence with this drug. Most of the studies used anthracycline based therapies in addition to the trastuzumab. In the BCGIRG-006 trial (published in the New England Journal of Medicine by Slamon 2011), 3,222 patients with metastatic breast cancer randomized to AC-TH or TCH. The first two contained doxorubicin (A), an anthracycline. The last two contained trastuzumab (H). The outcome was the same for patients treated with either anthracycline-given chemotherapy with trastuzumab (AC-TH) or taxane-based chemotherapy with Herceptin but without anthracycline (TCH). There was improved overall survival and disease free survival for all patients who received Herceptin and there was improved disease free survival in patients with positive lymph nodes as well as those with 4 or more positive lymph nodes. There did not appear to be a difference between the AC-TH and TCH arms. Further, there were only 7 cases of leukemia, 6 of which were in the anthracycline arms and one that was in the TCH non-anthracycline based arm of the study. However, the one patient in the TCH arm developed leukemia 20 months after she was treated for a B-cell lymphoma with an anthracycline. It was also noted that the patients with a history of congestive heart failure events were the patients who were treated both with trastuzumab and anthracycline.

There continues to be many unanswered questions regarding HER2+ disease. For example, is trastuzumab better given concurrently with chemotherapeutic agents such as doxorubicin (AC) in the postoperative setting or is it better to give it before surgery and then use chemotherapy after surgery? The idea behind the latter is that the first round of chemotherapy would before surgery would render the tumor cells more susceptible to the second round of chemotherapy because they would be more metabolically stressed. However, the N9831 study showed that concurrent treatment works better than after chemotherapy. Many researchers question what is the optimal length for treatment works better than after chemotherapy. Many researchers question what is the optimal length for treatment. It was noted that many of the patients who had the greatest risk of congestive heart failure events were the patients who were treated both with trastuzumab and anthracycline.

There are current questions regarding HER2+ disease. For example, is trastuzumab better given concurrently with chemotherapy or sequentially? The N9831 study shows that concurrent treatment works better than after chemotherapy. Many researchers question what is the optimal length for treatment. It was noted that many of the patients who had the greatest risk of congestive heart failure events were the patients who were treated both with trastuzumab and anthracycline.

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There are many new treatments being investigated to treat breast cancer patients with HER2+ breast cancer or in combination with trastuzumab (Herceptin). For example, lapatinib (Tykerb) targets both the HER2 receptors and the EGFR receptors. It is an oral agent that is FDA approved for metastatic HER2+ breast cancer that has progressed on Herceptin. Recent studies of lapatinib given prior to surgery suggest that it does treat the breast cancer, reducing the tumor and lymph node involvement. In addition, because it is a small molecule, it may cross the blood brain barrier and may have a positive effect on brain metastases downstream in the patient’s development. It is currently being evaluated in trials for use in early stage HER2+ breast cancer. TDM1 is a promising new HER2-targeted therapy that links a powerful chemotherapy agent to trastuzumab to provide more direct action to kill breast cancer cells. Pertuzumab, the focus of new clinical trials, is a specific monoclonal antibody that binds in special ways and disrupts signaling. A recent phase II study looked at its effects when combined with trastuzumab in the neoadjuvant populations. It had a much better side effects profile because patients were not getting chemotherapy at all. Everolimus targets mTOR, which is a key regulator of a pathway stimulated by HER2, and disrupts signals downstream in HER2+ breast cancers. The outlook for these new agents and combinations of treatments with HER2+ breast cancer is positive. Each year there is more research looking at how these new agents work alone and/or in combination with both newer and older targeted treatments.

Triple Negative Breast Cancer

Triple negative breast cancers are those that test ER-, PR- and HER2- . They account for about 10-18% of all breast cancers. They are not synonymous with basal-like breast cancer, as 10-30% are not basal-like cancers. Basal-like breast cancer is defined by a gene expression profile and account for about 14-16% of breast cancer. 15-40% of these are ER-, PR- or HER2-. There are a variety of markers that are used to identify basal type tumors; however, there are no standardized cut-offs for the amount and different labs assess for these in different ways so they are not reliable at this time.

There are specific features that are common in triple negative breast cancers. They tend to be more aggressive with a high grade and a high relapse pattern, especially in the first five years. Most of the relapses are in the first 1-3 years. They also have a very low rate of recurrence 8 years after the diagnosis. They show a different pattern of sites for relapse than the luminal type of breast cancer and tend to metastasize to organs and to the central nervous system (brain). Patients who respond to neoadjuvant chemotherapy tend to have a good outcome similar to triple-negative breast cancer. Triple negative breast cancers tend to be more common in younger women, African American women, women who have BRCA1 mutations, and patients with BRCA pathway dysfunction. In addition, many triple negative breast cancers have PS13 mutations.

The challenge of triple negative breast cancer has been finding unique molecular characteristics and as a result, there is limited treatment options for this type of breast cancer. As a result, there have been no clear targeted towards which to direct treatment. Recently, however, there has been increased attention to targeting DNA repair pathways. When DNA damage occurs in normal cells, enzymes such as the DNA repair enzymes like UV radiation or chemicals, this can lead to a break in the double-strand of DNA. DNA repair proteins are then called to the site of damage to repair the DNA. The primary proteins responsible for double-strand DNA repair are BRCA1 and BRCA2. These are essentially error-proof pathways of DNA repair. In some patients, however, an inherited genetic mutation in BRCA1 or BRCA2 (or another problem leading to poor BRCA1/ BRCA2 gene function) leads to underproduction of the proteins that have DNA damage have a lower probability of correctly repairing the DNA and a higher chance of mutations occurring. Mutations can lead to the development of uncontrolled cell growth or cancer. PARP is an acronym for poly (ADP-ribose) polymerase which is a protein that has several roles in the repair of DNA that is important in damaged cells. PARP is a protein used to repair DNA single-strand breaks. A patient with a low level of BRCA1 or BRCA2 protein expression (poor double strand DNA repair) will have a high risk of tumors developing, but the tumor cells can survive because they have PARP to help them hobble along. Scientists then theorized that if you take this patient with no BRCA1/2 function and give them a drug to block the function of PARP, single strand DNA breaks will convert into double strand breaks (which cannot be repaired without BRCA1/2). The tumor cell can no repair the double strand break or single strand breaks and the tumor cells die. Triple negative and BRCA cancers have a high level of cell death with BRCA may be lost or non-functional in the absence of BRCA mutation in sporadic triple negative cancers. Preclinical evidence suggests that inhibiting DNA repair mechanisms (e.g. PARP) will be most effective in tumors lacking functional BRCA1 or BRCA2 protein. Approximately 30%, a significant proportion of all breast cancers, lose BRCA expression though epigenetic mechanisms rather than mutations supporting the testing of PARP in this patient population.

With this knowledge and theory in mind, an initial study of a PARP inhibitor BSI-201 was tested in a randomized phase II trial in combination with gemcitabine and carboplatin compared to the gemcitabine/carboplatin regimen alone. The trial enrolled 123 women with triple negative breast cancer. The preliminary efficacy results showed a significant objective and clinical response, as well as improved progression free survival and overall survival for the patients who received the PARP inhibitor. Unfortunately, the 400 patient phase III study evaluating BSI-201 did not meet its primary endpoint; thus it does not appear to be beneficial in the way it was initially expected. However, this first PARP drug is a relatively new molecule and there are other stronger targeted approaches being evaluated (such as c met inhibitors) for this type of breast cancer.

The Future

There is no question that treatment strategies for breast cancer have changed substantially in the last 10 years. There are more options and, even more importantly, there are more clinical trials than ever before that will continue to answer many of our current questions as well as unanticipated questions. The targeted treatments have led to changes in treatment options at all levels of the continuum of breast cancer from early stage disease to late stage disease. For the first time, mutated cancer have similar biology and behavior. It had a much better side effects profile because patients were not getting chemotherapy at all. Everolimus targets mTOR, which is a key regulator of a pathway stimulated by HER2, and disrupts signals downstream in HER2+ breast cancers. The outlook for these new agents and combinations of treatments with HER2+ breast cancer is positive. Each year there is more research looking at how these new agents work alone and/or in combination with both newer and older targeted treatments.

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Encourage your friends and family to log on each month and see our lecture. Of course, we hope you will join us because then you get to ask your questions and we love seeing you there!

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<th>June 12, 2012</th>
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<td><strong>BREAST CANCER TREATMENT 2012: SURGICAL AND MEDICAL PERSPECTIVES IN DIAGNOSIS, TREATMENT AND RECURRENCE PREVENTION</strong> - Raquel Prati, MD, UCLA Assistant Clinical Professor and breast surgeon, and Olga Olevsky, MD, UCLA Assistant Clinical Professor and medical oncologist, discuss the evolution of breast cancer treatment from both surgical and medical oncology perspectives. Important surgical considerations are discussed including lymph node dissection vs. sentinel node biopsy for staging and therapeutic purposes along with potential complications such as lymphedema. Breast cancer often requires multimodal systemic therapies such as hormonal treatments, chemotherapy and targeted therapies. These treatments along with new molecular classifications, prognostic assays, such as MammaPrint® and Oncotype DX® used in treatment decisions, are also discussed along with recommendations for diet, exercise and vitamin D in the prevention of breast cancer recurrence.</td>
<td><strong>ADOLESCENT AND YOUNG ADULTS (AYA) AND CANCER: TREATMENT AND SURVIVORSHIP</strong> - Herbert Erstad, MD, UCLA Assistant Professor of Medicine and medical oncologist/ hematologist, Jacqueline Casillas, MD, UCLA Associate Clinical Professor of Medicine, pediatric medical oncologist/hematologist and Associate Director UCLA LiveSTRONGtm Survivorship Center of Excellence, Kaiser Ahmed, PhD, staff psychologist and Thomas J. Past, LCSW, oncology social worker Simms/Mann - UCLA Center for Integrative Oncology tackle the wide range of concerns of individuals diagnosed with cancer during the age range of 15-39, also known as adolescents and young adults with cancer or AYAs. This panel, presentation, and Q &amp; A considers the biology of AYA cancers, history, and research as well as distinguishing important issues that are unique to the AYA population both during treatment and through survivorship. Both medical and psychological issues, as well as support options and resources, are addressed. Both AYAs and their families are encouraged to attend as topics such as treatment management, fertility, late effects, psychological distress, emotional support and research needs and actions are brought together by this team of experts working at the forefront of AYA and cancer.</td>
<td><strong>CANCER-RELATED EMPLOYMENT AND INSURANCE ISSUES: WHAT ALL PATIENTS AND CAREGIVERS NEED TO KNOW</strong> - Director of the Cancer Legal Resource Center, Loyola Law School, discusses the most common cancer-related legal issues for cancer patients and survivors, including: health insurance and health care options; employment rights and reasonable accommodations in the workplace; taking time off work; and access to disability insurance and government benefits. He covers the ways that the Affordable Care Act and the latest health care reforms apply to people coping with a cancer diagnosis.</td>
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<td>July 10, 2012</td>
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<td><strong>SURVEILLANCE VS. TREATMENT FOR PROSTATE CANCER</strong> - Leonard S. Marks, MD, Professor of Urology, urologist and researcher, discusses how MRI imaging (to visualize localized prostate cancer) and ultrasound guided biopsy (via the new device Artemis) are being utilized at UCLA and changing the way we treat prostate cancer. He discusses how “active surveillance,” an organized follow-up for men believed to have a ‘low-risk’ prostate cancer, is an important potentially, quality-of-life improving approach to prostate cancer care. He also presents current more aggressive treatment methods for higher risk prostate cancer.</td>
<td><strong>PANCREATIC CANCER 2012: SURGICAL AND MEDICAL TREATMENT</strong> - Timothy R. Donahue, UCLA Assistant Professor of Surgery and Molecular and Medical Pharmacology and gastrointestinal and pancreatic surgeon, and Zev Wainberg, MD, UCLA Assistant Professor, medical oncologist and Assistant Director - GI Oncology Program, discuss surgical and medical treatments for pancreatic cancer. Pancreatic cancer is a common cause of cancer-related death for both men and women in the United States. When caught early, it can occasionally be cured. Treatments include surgery, radiation therapy, chemotherapy and novel biologic agents. A comprehensive overview of the treatment of pancreatic cancer is discussed, including recent clinical trials with improved survival for patients with advanced-stage disease.</td>
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<td><strong>MAKING SENSE OF NUTRITION AND SUPPLEMENTS IN CANCER</strong> - Karen Duvall, MD, MPH, Assistant Clinical Professor, Associate Director of the Preventive Medicine Residency Program at UCLA, discusses nutrition and supplements and the controversies that sometimes arise as recommendations change. Recent research identifies certain foods and supplements that may be important in the prevention of cancers as well as the prevention of recurrence, which are discussed along with how to integrate supplementation into a plan for a healthy diet. Mary Hardy, MD, Medical Director of the Simms/Mann-UCLA Center for Integrative Oncology, discusses complementary therapies and how to identify high quality supplements and choose complementary therapies.</td>
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<td><strong>LUNG CANCER 2012: TRADITIONAL AND NOVEL APPROACHES</strong> - Jay M. Lee, MD, Surgical Director – Thoracic Oncology Program, UCLA Assistant Professor, thoracic surgeon and researcher, and Edward Garon, MD, Co-Director of Medical Oncology Program - Thoracic Malignancies, UCLA Assistant Professor, medical oncologist and researcher, discuss the role of surgical treatment and non-surgical interventional procedures, chemotherapy and targeted therapy for early and late stage lung cancers. He presents new treatment options, including targeted therapies for lung cancer. Clinical trials at UCLA and the rationale behind those studies are also addressed.</td>
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REFLECTIONS ONLINE STORE

Reflections® is a boutique that provides information, resources and products to help men, women and children manage the physical appearance changes caused by cancers and their treatments. Our staff are certified fitters of mastectomy bras, prostheses and lymphedema garments and have many solutions for hair loss.

Reflections® is located in Suite 163 on the ground floor of the 200 UCLA Medical Plaza. It is open to the public Monday –Thursday from 10am-5pm, Fridays from 10am-3pm. Please call to verify our hours.

Reflections® is a not-for-profit organization committed to providing an array of affordable services and products. Proceeds from the sale of goods support Reflections’ daily operations and those of the Simms/Mann-UCLA Center for Integrative Oncology.

Many insurance companies provide partial to complete reimbursement for breast prostheses and some lymphedema garments. Reflections® is a preferred provider of breast prostheses and bras for Kaiser-Permanente, Blue Cross, Blue Shield, the University of California Medical Group and others. We also are a Medicare provider. We can assist you in obtaining authorization for covered services.

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