CHAPTER TWO
WHAT CANCER IS

Drs. Aubrey Pilgrim, E. David Crawford
and Several Contributors

Cancer is one of the most fearsome words in our language. Some people equate it to a death sentence, but many cancer patients live longer than those who have never had cancer. One reason is that they begin to start taking better care of themselves. If discovered in time, many cancers can be cured or treated so that the person can live a fairly normal and extended life.

Each year, over 1,500,000 people are diagnosed with some type of cancer. One out of every two men and one out of every three women will be diagnosed with some type of cancer in their lifetime. About 80 percent of these cancers are preventable because they are due to four major factors: Lifestyle, which includes smoking, diet and infectious agents; Workplace which includes chemicals, fibers and radiation; General Environmental contaminants in air, water and food; Clinical and other medications and radiation. All of these factors combine with the patients age, gender, ethnicity, genetics, nutrition, immune function and any preexisting disease to cause cancer.

Frederica P. Perea wrote an article for the May 1996 issue of Scientific American Magazine titled Uncovering New Clues to Cancer Risk. The investigator says that there are over 400 chemicals that have been shown to be carcinogenic in humans and animals. Many of these carcinogens are in our air, water, food supplies and the workplace. If we could eliminate environmental exposures, it is estimated that cancer incidence could be reduced by 90 percent.

The deaths of most of those 560,000 people, who die each year due to all types of cancer, could be prevented if the cancer is detected early. **The answer to cancer is early detection.**

The Most Common Cancers

Skin cancer is the number one diagnosed cancer, but it is fairly easy to treat and does not kill many people. Lung cancer is still the number one killer of men and women. It kills about 150,000 men and women each year. There are about 180,000 cases of prostate cancer diagnosed each year and it kills 30,000 to 40,000 men each year. Breast cancer is the fourth most diagnosed cancer with about 180,000 detected each year. About 43,000 women die from it each year.

Just a few years ago, there were more incidences of diagnosed breast cancer than prostate cancer. But more men are now being made aware of prostate cancer and are concerned enough to get a check up. However there are still a

large number of men who have the disease and are not aware of it. At least one man out of every ten over 50 has prostate cancer. For black men, the risk is even higher. One out of every eight black men over 50 will have prostate cancer. At this time, there are about 40 million men in the U.S. over 50. This means that there are over four million men with prostate cancer. For many of these men, the cancer will never become significant.

Before 1990, the incidence of diagnosed prostate cancer was about half what it is today. Even the number of men who died from it was less. Before 1985, the primary method of prostate cancer diagnosis was by digital rectal exam (DRE). This is the test that the doctor does when he has you bend over and he or she puts his gloved finger in your rectum. The prostate can be felt through the rectal wall. About 70% of all prostate cancer is the area that can be felt through the rectal wall.

Today we have the prostate specific antigen (PSA) blood test which is much more accurate in detecting prostate cancer. So many more cases are being diagnosed. One reason more men are dying from prostate cancer today in spite of the early diagnosis, is because fewer men are dying from heart disease, lung cancer and other diseases. Many men are now living long enough for their prostate cancer to kill them.

We don't know how to prevent cancers, but most of them can be easily cured if they are discovered early. Usually a breast cancer or prostate cancer that is found early is fairly inexpensive to treat and cure. But if the cancer is advanced when first detected, it can be treated, but it is incurable. It is also very expensive to treat. Doctors can offer palliative treatments to ease the pain and to try to keep the patient as comfortable as possible. In many cases, even with metastatic cancer, the patient can live a fairly good life. Of course the quality of life can never be the same. We will say it again and again, the best way to fight cancer is an early checkup and early detection.

Family Risks

We have known for some time that there is a definite familial risk among close male family members for prostate cancer. Some studies have indicated that close female relatives of men who have prostate cancer have a higher risk of getting breast cancer. It works both ways so male relatives of women who have breast cancer have a 40% to 50% higher risk of prostate cancer.

Men over 40 should have a prostate checkup at least once a year. Women over 40 should have a breast cancer checkup at least once a year.

CANCER TERMS

There are several terms that you may not be familiar with. We have a comprehensive glossary in the Appendix. Here are a few of the common terms that we will be discussing in this chapter.

Cancer
Cancer is the abnormal and uncontrolled growth of some of the cells in a body. About 90% of cancers are called carcinomas. Some of the others are called sarcomas, which are usually found in connective tissues; osteomas, or bone cancer; melanomas, or cancers from moles. Cancer is from Greek which means crab.

Tumor
Tumor is Latin, meaning a swelling. The -oma in carcinoma is a Greek suffix that means tumor. So cancers may also be called tumors, but not all tumors are cancerous. Some tumors are benign growths or lumps that may not be life threatening.

We want to stress the fact that **the first rule about cancer is that there are no rules**. Quite often, but not always, the cancer will be a hard lump. Ordinary cells usually have spaces between them filled with lymphatic fluid and the tissue is rather soft. Many cancers are hard lumps because the cells are packed very close together. A cancer tumor may have ten times more cells than an equivalent amount of normal tissue.

A tumor may also be called a neoplasm. Neo is Greek for new and plasma is Latin for form or mold. A neoplasm has come to mean a new and abnormal formation of tissue.

The term carcinoma is derived from the Greek karkinos which means crab. The ancient physicians of the Hippocratic school thought that the cancer they saw in their patients looked like a many legged crab. The grasping branches of the cancer that spread out reminded them of the claws on the crab.

Cancer is like a parasite. A parasite is an organism that lives within or upon a host. It contributes nothing to the benefit, welfare or survival of the host. Parasites may be such organisms as fleas, lice, tapeworms, fungi, bacteria, and viruses. Often the parasites will become so greedy that they will suck the life right out of the host. Cancer can do the same.

Metastasis
Metastasis is from Greek- meta means after, beyond, or over- stasis means to stand- So metastasis means to stand beyond or over.
As long as a cancer remains encapsulated as a tumor, it may not be much of a problem, unless it is growing on or in a vital organ such as the brain. But it becomes an incurable problem when the cells begin to spread and metastasize. The cancer may send out fingers and invade nearby tissues. Normal tissue does not invade neighboring tissues.

A few cells may break away and escape in the blood stream. These cells may then set up a distant colony. If the cells came from the prostate then it will still be prostate cancer even if it is located in distant areas of the body such as the lymph nodes or the bones of the spine.

Digital Rectal Exam (DRE)
Part of the prostate can be readily felt through the rectum. An experienced doctor can do a digital rectal exam (DRE) and determine if there is any unusual growth or abnormality. A normal prostate is fairly soft and uniform. If there is prostate cancer present, depending on the stage and location, it may be hard or indurated, which means hardened. It may have lumps and nodules. If there seems to be any abnormality, the doctor may have a PSA test done, then perhaps ultra sound tests and a biopsy.

A DRE and a PSA test can detect most all prostate cancer. Most prostate cancers are slow growing and may not cause any problem as long as they remain encapsulated in the prostate. If they live to an old age, most all men will die with prostate cancer, but not necessarily because of it. It has been estimated that 80 percent of 80 year old men have prostate cancer to some degree. If a man lives to be 100 years old, the chances are about 100 percent that he will have prostate cancer to some degree. Many of the cancers found in these cases may still be contained within the prostate capsule and have not caused any problems.

Prostate Specific Antigen (PSA)
It is difficult to think of anyone having cancer as being fortunate. But prostate cancer patients may be considered fortunate in that the cancer creates a substance that can be readily detected. The prostate produces Prostate Specific Antigen (PSA) that is present in the blood stream. If cancer is present, the amount of PSA will usually be elevated. Quite often the amount of PSA in the blood will correspond roughly with the amount and size of the tumor. Usually the more tumor cells, the more PSA is present. A blood test for PSA may cost less than $50, which is very inexpensive when you consider that it could save a person’s life.

Once the prostate has been removed there should be no PSA in the patient’s blood. If PSA is still being produced then we know that the operation was not done soon enough to prevent metastasis. Cancer that has metastasized to some other part of the body may be treatable but not curable. Knowing that cancer is still present, the doctor has several methods and treatments to control it as much as possible.

Angiogenesis
When you think about it, setting up a distant colony is a remarkable feat. This cell, or a few cells, float around in the blood stream, then find a suitable spot and settle down. A few cells can exist for a while by diffusion of nutrition from existing

blood vessels. But as they multiply and grow they need an ever increasing and constant supply of blood to bring oxygen and food for their voracious appetites. But the lack of blood vessels is not much of a problem for the pioneer cells. They simply secrete substances that the nearest blood vessels pick up. These substances, Vascular Epithelial Growth Factors, (VEGF), cause the nearby blood vessels to create a new path to the metastatic colony. This is called angiogenesis. (Angio is from the Greek, meaning vessel, -genesis is from the Greek meaning generation or birth).

Over 40 angiogenesis-inducing compounds have been identified. Several anti-angiogenesis compounds have been discovered. These substances seem to work well in stopping cancer growth in animals. Lots of promising research is being done.

Oncologist
An oncologist is a doctor who specializes in the management or treatment of cancer. Onkos is from the Greek, which means tumor or mass.

Adenocarcinoma
Adeno- means gland. Since the prostate is a gland, prostate cancers are called prostatic adenocarcinomas. An adenocarcinoma could occur in any gland, such as the adrenals, the thyroid or the pancreas. A gland is usually an organ or structure that produces and secretes substances that may be used in other parts of the body.

Chromosomes
Your body is made up of several trillion very tiny cells. The cells have a central nucleus which contains the chromosomes, protoplasm and other structures. The chromosomes carry the 100,000 genes that determine the characteristics of the person. There are various numbers of chromosomes in the cells of different plants and animals. In the human, there are 23 pairs. These pairs of chromosomes are called diploid, which simply means twofold. Diploidy means that the cells have two sets of homologous chromosomes. Homologous means that they are similar, such as your two hands are similar.

Some cancer cells do not have the characteristic pairs of chromosomes. Some of them may be aneuploid, (the prefix an- means without or not, eu means good), which means that the cells are not good and do not have the normal pairs of chromosomes. A single cancerous tumor may have several different ploidy types of cells. Ploidy tests can be done on biopsied material from a tumor to determine the ploidy. Those tumors that have a high percentage of aneuploidy usually have a poor prognosis. (Prognosis is Greek meaning foreknowledge. It usually means a prediction of an outcome of a disease).

Cancer Prevention

We still don't know all of the factors involved in the causes of cancer. Of course you need to avoid the known carcinogens. Until we fully understand the causes of cancer, it is difficult to completely prevent it. That is especially so for prostate cancer.

A dietary study of 47,000 men over a six year period, done at Harvard, was published in the Dec. 1995 Journal of the National Institute. It showed that men who eat at least ten servings a week of tomatoes or tomato based foods such as pizza and spaghetti sauce were 45% less likely to develop prostate cancer. It is the lycopenes in the tomatoes. Several other vegetables also contain lycopenes.

Some studies have linked high animal fats to breast and prostate cancer. There are several different types of fats. Dr. Charles Myers, who wrote part of Chapter 19 on Diet and Exercise, has done a lot of study on the various types of fats. Check out what he has to say about the various types of fats.

Low levels of minerals such as zinc and selenium have been cited as a possible cause of prostate cancer. Dr. L. C. Clark did a comprehensive study on selenium, His study indicated that 200 ug or selenium per day could help prevent prostate cancer. Selenium supplementation may reduce the risk of certain cancers, according to a study published in the Dec. 25 1997 issue of the Journal of the American Medical Association (JAMA). The study included data on 1,312 patients over a 10-year period. While there was no decrease in skin cancers, there was a 40 percent decrease in overall cancer risk, with marked decreases in the incidence of lung, colorectal and prostate cancer. To find out more about selenium studies, go to http://www.yahoo.com or any of the other search engines, and search for selenium AND prostate cancer. You can use the search engines to find data about almost any thing you would like.

Testosterone levels may also be suspect in the cause of prostate cancer. The oriental men usually have a fairly low level of testosterone compared to Caucasians. Black men usually have a rather high level. We know that prostate cancer is dependent on testosterone. If a male is castrated early in life, he will never have prostate cancer or benign prostatic hyperplasia (BPH).

One of the most effective treatments for prostate cancer that has metastasized is castration. (A more euphemistic term is orchiectomy, but it means the same thing.) A less harsh treatment is to use drugs that chemically counteract androgenic hormone productions and bring them down to castrate level. These drugs are usually very expensive compared to orchiectomy. But most men had rather hold onto their family jewels because they represent manhood. Even if the testicles are nothing but a useless ornament that no one will ever see, they still want to keep them. Besides, maybe they will get lucky and their cancer will go into remission. Or someone will come up with a magic bullet, a miracle cure.

There is a lot of variation in testosterone levels, by age and even daily. The highest levels are usually in the morning. On average, testosterone levels change with age. The highest level is from about 15 years old up to 30 years old, then it starts dropping. The levels may range from 400 ng/100 ml (nanograms per milliliter) up to 1100 ng/100 ml at age 30. At age 70 it may range from 200 ng/100 ml up to about 600 ng/100 ml. For men who are undergoing combined hormone therapy (CHT), the goal is to bring the testosterone level down to 20ng/100ml or less. This is considered to be castrate level.

Prostate cancer is related to testosterone but it seems strange that more men get the cancer when they are older and the testosterone levels are normally decreasing. In a similar manner, more women get breast cancer after they have experienced menopause and are no longer producing estrogen. One possible reason could be that the beginning prostate cancer and breast cancer may have started several years earlier when the person was producing large amounts of the hormones.

Several genetic studies are being done to find new methods of early detection of certain cancers. The researchers can look at the genes and detect differences that may pre-dispose the person to cancer long before it becomes evident. But several questions have been raised. What happens if a person is told that they have a high risk of developing cancer and he or she tries to buy health insurance? What happens to their employment? What will be the rules of privacy? What happens to his state of mind if he is told that he will die an early death because of cancer?

Dr. David Bostwick, and others, have found that there is a precursor to prostate cancer that can be detected by a biopsy. The biopsy may not detect any cancer, but some of the cells may show that they are changing and undergoing Prostatic Intraepithelial Neoplasia (PIN). In some cases it may be more evident than in others and may be classified as High Grade PIN or HGPIN. Dr. Bostwick says that HGPIN almost always develops into prostate cancer. He has treated some of his patients who had HGPIN with Proscar and Casodex and they do not progress to prostate cancer. There have not been a lot of studies done yet, but it would seem to be a very good way to prevent prostate cancer.

How We Start Life

We first start life as a single cell that results from the uniting of a single sperm from the father and an egg from the mother. Neither the sperm nor the egg is a complete cell by itself. Every cell in our body has 46 chromosomes except that the sperm and egg cells have 23 chromosomes each. When the sperm and egg unite they form a complete cell which will have 46 chromosomes. (Different animals and plants may have a different number of chromosomes.) The chromosomes contain the genetic material, inherited from each of your parents, that determines who you are and what you are.

Once the sperm and egg have united, almost immediately the single cell begins to divide and multiply. It divides into two complete cells, these two become four, the four become eight. Soon the single cell that resulted from the union of the sperm and egg becomes an embryo that has millions of cells.

To give you an idea of how cells multiply here is an old problem. It asked, “Which would you choose, to be given one million dollars outright, or to be given a single penny, then have it doubled each day for 30 days?” Without doing the simple math, many people would say they would rather have the million dollars. But if you are given one penny on the first day, then two on the second day, four on the third, and continue to double the amount each day, on the 30th day the single penny doubled each day would amount to $5,368,709.12. On the 31st day the amount would be $10,737,418.24.

The cells in the embryo may double and multiply even more often than once a day, so it is easy to understand how one cell can quickly develop into trillions. But the fast growing cells in the developing embryo are strictly regulated and controlled. After the baby is born, the cells continue to rapidly grow and multiply until the person reaches adulthood when normal growth is stopped and cells will only be produced to repair or replace damaged or worn out tissues. At this time the body will be made up of the several trillion cells.

Differentiation

The body is made up of several different cells, organs and tissues. All of these different cells are derived from the single cell that resulted from the fertilized egg. As the embryo grows and develops, the cells change, or **differentiate**, into whatever cell type is needed for a particular tissue or organ.

It is interesting to note that some plants and lower animals retain a large amount of undifferentiated cells throughout life. There are so many undifferentiated cells in some plants, such as the geranium, that all you need is a small piece of a branch to grow or clone a complete new plant. Some lizards can lose a part of their tail or a foot to a predator and the tail or foot will eventually regrow from embryonic type undifferentiated cells. If we could find out how the lower animals do this, perhaps humans could do it. Studies are being done using human embryonic tissues, even though some people are protesting such studies.

When a cancer develops, the cells may have several different shapes and forms. Some of the cancer cells may be very similar to the original prostate or whatever type of tissue it derived from. These cells would be called well differentiated. Some of the cells within the tumor may not have any resemblance at all to the original cells. These would be called poorly differentiated or undifferentiated. Between these two extremes might be some moderately differentiated cells. The process of cells becoming poorly differentiated or undifferentiated is sometimes called dedifferentiation.

Most prostate cancers may have a mix of many different stages of differentiation. The Gleason Score for staging prostate cancer is based on the mix of the differentiation of the cells. We will discuss the Gleason Score in Chapter Six.

Ordinarily, those tumors with a large number of poorly differentiated cells are the more aggressive and dangerous. They grow faster and metastasize early. They usually have a worse prognosis than the well differentiated type tumors. But this is not always the case. There are no hard and fast rules that are etched in stone when it comes to cancer. Again, the only rule regarding cancer is that there are no rules. There are exceptions and sometimes the poorly differentiated tumor may grow no faster than a tumor that is well differentiated. And sometimes the well differentiated may become aggressive and fast growing.

Four Basic Functions of Life

Together, our many cells form a complete system or person. There are four basic functions that we all do. We eat, we digest the food, we eliminate the waste and we reproduce. Each of the individual cells in your body performs the same basic functions. Food and oxygen is brought to each cell by the blood stream. The cell takes in the nutrition, digests it, then throws off the waste products into the lymph system, the clear fluid that surrounds each cell.

Each individual cell has a purpose and a job to do. Depending on what part of the system they are, every one of our cells perform specific functions that keep us alive. For instance the cells in the lungs take the oxygen that we breathe in and throws off the carbon dioxide waste. The cells of the stomach and intestines produce enzymes and chemicals to help break down and digest the food we eat so that it can be used by the various other cells of the body. Cells in glands such as the pituitary, the adrenals, the ovaries and testes produce hormones that are vital to us in controlling our bodies.

Even the lowly cells that make up our skin have several purposes and functions. Among the many jobs the skin does is to cover and protect our vital organs. It helps to protect us from the invasion of infectious organisms. It also acts a barrier to many chemicals and toxic materials. It contains many of the sensory nerve fibers that allow us to feel and to be aware of our environment. It helps maintain body temperature by perspiration and has many other functions.

The Blood and Lymph System

In order for any cell or tissue to survive and grow it must have a constant supply of food and oxygen. There must also be a means to remove the waste products. The blood and lymph system perform these tasks.

The heart circulates the blood through the lungs where it throws off waste carbon dioxide and picks up oxygen. It pumps the freshly oxygenated blood out to all of the tissues and cells of the body, drops off the oxygen and picks up the waste

carbon dioxide. Some of the blood is also circulated around the intestines to pick up nutrition and deliver it to the cells that need it. The blood stream also picks up hormones and enzymes and delivers them to the tissues where they are needed.

When the blood leaves the heart, it is under a considerable amount of pressure. The arteries leaving the heart are fairly large. But as they branch down into the very small capillaries there is very little pressure left when they connect to the venous blood vessels. The venous blood vessels rely primarily on a one-way valve system to get the blood back to the heart. Most veins have muscles near them or that surround them. When a muscle is contracted it squeezes on the vein and forces the blood toward the heart. When the muscle is relaxed, the blood may try to fall back, but a small flap or valve in the vein closes and prevents the blood from going backwards.

The lymph system is a system of vessels very much like the venous system. The vessels have one-way valves much like the veins. A major difference in the veins and the lymph system is that the blood system is a closed system, the veins connect directly to the arteries through the capillaries. The lymph system is open on the collecting end. The cells dump the waste, or end products of digestion and metabolism, into the surrounding lymph fluid.

Much like the venous system, when a muscle is flexed, the lymph fluid is forced through the one-way valves of the lymph vessels. This waste material is dumped into the venous system near the heart.

Lymph Nodes

One of the tests to determine whether a cancer has metastasized is to examine the nearby lymph nodes. The lymph system is somewhat similar to the drainage system of our streets. When it rains, water flows into drainage pipes below the streets. Steel grates filter out the large waste materials. In our lymph system, a series of nodes filter out bacteria and any foreign agents to prevent them from getting into the blood stream. The lymph nodes produce special cells that can kill off bacteria and help maintain the body's immune system. Quite often the lymph nodes will become enlarged whenever a person becomes ill. The nodes will produce large numbers of killer cells to try to protect the body.

How Cancer Spreads

Whenever cancer starts to spread, some of the metastatic cells are often stopped temporarily by lymph nodes. But the cancer cells usually don't cause enough alarm to cause the lymph nodes to stop them completely. The lymph nodes may become overwhelmed and the cancer cells may proceed on their way to set up new colonies or tumors. In prostate cancer, quite often the new metastatic tumors are formed in the bones of the spine.

When a radical prostatectomy is performed, ordinarily, the lymph nodes

are examined first for cancerous cells. A microscopic examination of the lymph nodes can often reveal whether a cancer has metastasized. Sometimes a laparoscopic examination will be done before the operation. Or the surgeon will take out the lymph nodes and have a pathologist examine them immediately.

If any cancer cells are found in the lymph nodes, it means that the cancer has already spread. In this case, it usually doesn't help to remove the prostate. Like the old saying, it's not much use locking the barn door after the horse has escaped. Most doctors will sew the patient back up and start him on other therapy. However, a recent study reveals that removing the prostate and starting the patient immediately on hormone therapy improves survival when compared to removing the prostate and delaying hormone therapy.

The cancer cells may also escape through the many blood vessels that enter and leave the prostate. A prostate cancer cell may be no bigger than a blood cell, so it would be no problem to travel along with them.

There are also lots of nerves that enter and leave the prostate. Quite often perineural invasion is found in removed prostates. Which means that the cancer cells were found migrating in the sheath that surrounds nerves. (Perineural- peri means around, neural means nerve.)

The other way for the cells to escape is through extension and invasion. Remember that cancer means crab. The cancer may send out fingers of cells that penetrate the prostatic capsule and enter the nearby pelvic organs such as the seminal vesicles.

As long as the cancer is contained, stays fairly small, and does not invade a vital organ, it may not kill the host. The cancer usually kills when it gets so large that it is an unbearable burden to the body. It can also kill when it invades an organ that is vital to life such as the lungs or brain. Often when it invades another organ, it usually grows to such an extent that it crowds out all of the normal cells. The cancer cells have a voracious appetite and may deprive the normal cells of any available nutrition.

Cancer may also kill by debilitation of the patient. They may not even be able to determine the source of the cancer, but the patient may become weak, lose weight and gradually fade away.

How Cancer Survives

At the present time when cancer is diagnosed we have no way of knowing whether it has already set up micrometastases somewhere in the body. We do know that if the PSA is 20 or greater and the Gleason score is more than 7, the cancer has probably already escaped the prostate gland.

Because we can't recognize early metastatic disease, some men are operated on needlessly. Some of these men may appear to have been cured, but within five years, metastatic cancer may become evident in up to 20 percent or more of men who were thought to have been cured. The final pathology report on the removed prostate and Gleason sum can sometimes predict who will fail.

Reverse transcriptase polymerase chain reaction (RTPCR) is a test that can detect cancer cells in the blood stream. But just being able to find a cancer cell in the blood stream is no guarantee that it will be able to find a suitable place to settle down, establish a colony and grow new blood vessels.

When cancer cells begin to proliferate, they must have lots of food and nutrition. To get it requires extra blood and lymph vessels. The ingenious cancer cells produce angiogenic factors that cause the body to create the extra blood and lymph vessels.

For every chemical, drug or hormone that causes an action, there is usually one that causes an opposite reaction. Scientists have discovered several of the tumor angiogenic factors. Several studies are being done with anti-angiogenic drugs that would inhibit the production of the angiogenic factors. By counteracting the angiogenic factors produced by the cancer cells, they would be denied a blood supply and nutrition and would thus die.

Oncogenes

There are about 100,000 genes in the 46 chromosomes of each cell. The genes are carried in the DNA and are the blue print of all the characteristics that were inherited from the parents. The genes determine the eye color, the person's size and shape and all of the characteristics of a person. Some studies have indicated that a few of these genes, about 100 or so, are oncogenes, or genes that can cause cancer.

The cells of our body normally reproduce or split exactly in half when it is necessary to replace or repair nearby cells or tissues. When oncogenes are "hit" by a carcinogen, then reproduces, the resulting new cells may be abnormal cancer cells. Some studies seem to indicate that it may take two or more hits to the oncogenes from carcinogens to cause cancer.

Cancer and Age

Another factor in cancer is the persons age. The older a person is, the more likely that the person's oncogenes have endured several "hits" in his or her lifetime. So it is more likely that the older person will develop cancer. This is especially so for most breast and prostate cancer victims who are usually over 50 years old.

But many younger people also get cancer. Quite often, when cancer develops in a younger person, it is usually very aggressive and more likely to metastasize. It

may be that the younger person sustained a direct hit from a strong carcinogen to their oncogenes. Another reason may be that the person, young or old, may have inherited certain genetic flaws that predispose the person to have cancer.

There are thousands of carcinogenic factors. We are besieged by them on every side, in our homes, the workplace, in the air we breathe, in our food and in the genes we inherited from our parents and ancestors. We may never be able to identify all of the carcinogens. Even if we could identify all of them, there is no way we could protect ourselves from them and still live a normal life.

DNA Repair

The body is a very adaptable machine. The older person's system may learn to adapt and live with several small doses of carcinogens. The DNA of a normal cell can repair the genetic damage if it is not too severe. It is when the body is overwhelmed that our defense systems break down and the body is overcome. One reason that radiation treatments kill cancer cells is that the cancer cells do not have the ability to repair the damage done to them.

Programmed Cell Death, Apoptosis

Remember that all of the many trillions of cells in your body are derived from the original egg and sperm cell. Remember that the cells in your body must constantly replace any damaged cells, the old worn out cells, and cells needed for growth. Some studies have indicated that there is a finite number of times the cells can reproduce. It appears that the cells are programmed to die when this limit is reached. Scientists have called it apoptosis. The upper age limit for man seems to be about 120 years. Inherited genes are a big factor. So is the environment the body is subjected to and many other factors.

When a cell dies due to injury or some toxic substance, there is often an alarm. It causes swelling, redness and other effects of the damage. This alerts the bodies defenses and macrophages and other large cells rapidly move in and clean up the dead cells. Apoptosis, or natural death does not cause any alarm but it does cause the macrophages and other cells to clean up and remove the waste products.

As we get older, the cells that have changed and adapted make us into a different person. Because we are in a constant state of change and flux, we are a different person each day of our lives.

How Cancer May Start

Our bodies are made up of several hundred trillion separate individual living cells. (A trillion is 1,000,000,000,000). Most of the cells are so small that thousands of them could fit in the space occupied by the period at the end of this sentence. Examples of cells are the skin cells, muscle cells, nerve cells and other cells that make up the different tissues and organs of the body.

The various cells form tissues, glands, organs and systems. Each cell, gland and organ has a purpose and a function. They all work together to form a complete system that sustains us and keeps us alive. All of these different cells are derived from the first complete cell that was formed from the sperm and the ovum. The sperm and the ovum each contributed 23 chromosomes to make the complete cell with 46 chromosomes. Each of the cells in our bodies, whether prostate, liver or lung each have copies of the original 46 chromosomes.

Occasionally some of the cells wear out, are damaged, or for some reason die off. Even the cells in a young baby may wear out or become damaged. Sometimes a large number of cells are killed off or attacked by an infectious or harmful agent. Our bodies are marvelous machines and we have several defenses. Unless the damage or the attack is overwhelming, we can usually overcome the injury and recover our health.

In most instances, the cells that are killed off or damaged are replaced by nearby cells. A nearby cell of the same type as those damaged or killed off, will simply split in half and become two cells. The normal cells will continue to divide and multiply until the damage is repaired then stop reproducing.

Occasionally something may happen to cause one of these reproducing cells not to divide exactly in half. A daughter cell may not get exactly half of the chromosomes. Or the chromosomes may be damaged in some way. The resulting cells are no longer like any of the normal cells in our body. Often, the body will recognize these aberrant cells and destroy them. Unfortunately, some of them may not be recognized and they begin dividing and creating more and more of the abnormal cells. The body stops the reproduction of the normal cell when they are no longer needed. But it has no control at all over the abnormal cancer cell growth.

The cancer cells do not perform any useful function. They contribute nothing to the system. They take more than their share of nutrition, often robbing the neighboring hard working cells of their nutrition. They are parasites that often grow so large that they squeeze the neighboring tissues and kill them off.

Normal cells have a definite life span with programmed death or apoptosis. From laboratory studies, it appears that normal cells can divide about 50 times before they die. But instead of living for a certain length of time, then dying off, cancer cells keep right on living and multiplying into new cells that refuse to die. They are, in effect, immortal.

One reason may be because of telomeres. There is a section called a telomere (telos is Greek for end, meros is part) at the end of the chromosomes. It appears from some studies that the telomere becomes a bit shorter each time a cell

divides. When the telomere decreases to a certain length, the cell dies from the programmed death called apoptosis.

Scientists have discovered that most all cancer cells cause an enzyme, telomerase, to be produced. Telomerase prevents the telomere from being shortened or affected when the cell divides. This appears to be what makes the cancer cell immortal.

Scientists have found telomerase present in 90% of all cancers. They hope that the presence of telomerase can be used as a marker for early detection of cancers. It might also be used to determine the aggressiveness of cancers. Scientists are searching for a substance that can counteract the telomerase enzyme. Without the telomerase, the cancer cells would eventually die off just like normal cells.

Cancer Growth

The transformation of a single cell into one million cells would be too small to be detectable by most methods. Remember the doubling of the penny, over one million cells would be created after only 20 doublings. After 30 doublings, the tumor would have over one billion cells and could be detected as a lump. After it had doubled 40 times, the tumor would have about 1,099,511,627,780 or one trillion, 99 billion, 511 million, 627 thousand and 780 cells. The tumor would weigh about two pounds.

Depending on the type of cancer, its location and how aggressive it is, it may take years for it to double 20 or 30 times and reach a size to where it can be detected. During this time, it may not cause any pain or alarm to the body. A tumor may only cause pain or dysfunction if it is located in or near a vital organ. In this case its presence may be detected before it has doubled more than 30 times.

Over 100 Different Forms of Cancer

One reason it is difficult to find cancer before it has spread is that cancer is not a single disease. Cancer can arise in any of the cells, tissues, glands or organs of the body. Over 100 different forms of cancer have been identified.

There is some indication that there may be at least three different and distinct types of prostate cancer. The most prevalent type is a latent form which may never cause any problems. These cancers have a very low PSA and a low Gleason score. The moderate type may have a Gleason score of 5 to 7 and a PSA up to 10. It can progress and may eventually kill one. The very aggressive type may have a PSA of 20 or so and a Gleason score of 8 to 10. Its PSA may have a short doubling time and it may kill within just a few years.

Origin and Growth

Cancers usually arise at a primary site such as the prostate gland, the lungs, stomach or intestines. Cancer may remain at its original site and simply grow into a small tumor. You may have it for years and never know it. Eventually it may become a large tumor.

A cancer patient needs to make sure that his or her body gets plenty of the proper nutrition every day. The patient must intake enough nutrition, not only to satisfy the greedy and voracious appetite of the cancer cells, but to also have enough left over to feed and repair the normal cells.

Unfortunately, in many cases of advanced cancer, the person may lose his or her appetite completely. It is believed that the appetite loss is due to some factor produced by the cancer cells. The patient loses weight and may be just skin and bones when the cancer finally overwhelms and kills them.

A Detailed Explanation of Metastases

Dr. Roger Sopher is with the University of North Dakota School of Medicine, Department of Pathology. He is a prostate cancer survivor and devotes a lot of time answering questions on the Internet. Like most survivors who post to the Internet, he lists his case history at the end of this post. The following is a question from Meir Pann and Dr. Sopher's reply:

<<Meir Pann said: My point is, in all these years, wouldn't an errant cell or two be released, to wander in this universe of me, and be established somewhere as a micro-metastasis? Couldn't we point to this possibility as a source of the large percentage of the failed RPs on "localized, contained tumor" we see years after the operation?>>

Here is Dr. Sopher's reply:
"You have it pretty close to right but as you might guess it is an incredibly complex set of interconnecting events. The basic idea is that a single cell develops the capability of malignant behavior through a series of mutations. Some of these mutations were passed down from precursor cells that had only a partial change in their genome and some occurred in the final stage of things.

One of the things that happens in cells that have become malignant is that they lose the normal mechanisms that screen the genome for mistakes. Without these screening mechanisms, additional mutations become even easier and more prevalent. The term used is that cancer cells are genetically labile which means that they are easily changeable. As the clones of malignant cells develop, subclones also are produced. Many of these have lethal mutations and they die. But some have mutations that give the malignant cells some selective advantage in growth. Generally when this happens the subclones are worse behaved than their progenitors. This is termed tumor progression.

Now, a malignant tumor can only achieve a size of a couple of millimeters without its own blood supply. This was shown by a surgeon, Judah Folkman, in the seventies. (Editor's Note: In 1998, Dr. Folkman proved that he could cure cancer in mice by using endostatin and angiostatin. Several human trials are ongoing at the present time. We are confident that it will cure some cancers in humans). The tumor is incapable of making blood vessels. But it does have the ability to co-opt the surrounding stroma (connective tissue) into producing blood vessels for it by releasing a number of chemical signals.

At the same time the tumor often causes a particular kind of inflammatory cell (the macrophage) to come into the area. Macrophages, when they are activated, also produce chemical signals that cause the formation of blood vessels. The net effect is that the cells that should be involved in killing tumor cells help produce what the tumor needs to grow - blood vessels.

Now that the tumor has its blood supply, it can achieve greater and continued growth. Additional subclones develop that have the ability to invade through the walls of blood vessels. Clumps of tumor cells then can break off and circulate. As they float along they are generally covered by a layer of plasma proteins and platelets that hides them from the immune system.

The tumor cells have receptors on their surface that can bind to specific sites on the endothelial surface (lining of the blood vessels) that allows them to grab on. In some cases the physical size of the tumor clumps stops their progression through the microvasculature on the basis of size and they form a plug.

Some tumors definitely have the ability to home to specific sites for reasons that are still not completely understood. For example prostate cancer cells like to go to bone as does breast cancer cells. Lung tumors like bone, the adrenal glands, the brain and many other sites.

We know that tumors shed cells into the circulation even before any metastatic sites can be demonstrated. This was shown nicely in the mid 80’s in breast cancer. Some women had no involvement in their regional lymph nodes. When their bone marrow was sampled at the time of surgery and then analyzed, between 15 and 20 percent of these women had cancer cells in their bone marrow. In a follow up, there was no good correlation between the women that had cancer cells in their marrow at the time of surgery and those that went on to develop progressive disease.

So the mere fact that tumor cells are in the circulation does not seem to be a good predictor of those that will develop metastatic disease. The reverse transcriptase polymerase chain reaction (RTPCR) test has been used to probe for circulating prostate cells in the blood stream. It is a very sensitive test. In theory one can pick up a single cell in a 10 ml sample of blood. The problem is, what does it mean? At this point, in my view, not much until some correlation with

progressive disease can be proved. UCLA has recently done a study of RTPCR and came to the same conclusion.

Some believe that a primary tumor may produce an angiostatin substance which may help keep other tumors in check. Angiostatin certainly exists and may explain the rare case in which metastatic sites “blossom” when the main tumor is removed or conversely regresses. However those events are not common.

One of the interesting things about tumor growth is that it is not a linear function. Work done at the Argonne National Laboratory has suggested that tumor growth follows a Gompertz curve which says that it starts off fast and then slows down fast. The slowing is thought to be on the basis of the intrinsically poor blood supply of most tumors. When a metastasis occurs, it tends to grow as a new colony and follows its own Gompertz curve. Therapies aimed at preventing the tumor from inducing angiogenesis are very exciting. They may not cure anyone of the tumor but they would, in theory, make its presence inconsequential.

Our knowledge of basic tumor biology is improving. With the advances in molecular biology we are starting to understand things that were not even dreamed of just a few years ago. As a cancer patient, it may not seem like it, but we are gaining in our war. However, we still have many battles to wage.”

Roger L. Sopher, MD
Dept of Pathology
University of North Dakota School of Medicine, Grand Forks, ND
58202-9037

This is Dr. Sopher’s digest of his PCa history:
“60 year old male. 1993 - PSA 3.4, 1994 - PSA 4.1, 1995 - PSA 4.6, 1996 - PSA 6.7. Negative DRE at all times. July 1996 TRUS - 11 mm area of lucency in left lobe, BX left lobe - adenocarcinoma Gleason 2+3=5. Right lobe - negative.
July 1996 Radical retropubic prostatectomy and pelvic lymphadenectomy.
Pathology - tumor in left lobe with slight extension over the midline. One margin microscopically involved, Gleason score 2+3=5. September 1996 - continent.
November 1996 - PSA - below limit of detection. DRE - negative.
As of late 2000, PSA is still undetectable.
Note: BX is shorthand for biopsy. DRE is Digital Rectal Exam.

Treatment Choices
If a person is told that he has cancer, even if it is a small slow growing one, it may cause a lot of worry and stress. He may insist on having it treated or removed. If the operation is done properly and early enough, the person may live longer than a person who has never had cancer. The reason for a longer life is that the person may start taking better care of himself.

If the cancer is fairly small, at T1a or T2b stage and the biopsy shows a low

Gleason grade, the doctor may recommend that the tumor just be closely watched and monitored. If there is any change in the PSA or the other prostate tests, then treatment can be instituted immediately. If the person is over 75 years old, and the cancer seems to be growing fairly slow, the doctor may also recommend that it just be watched and closely monitored.

If it appears that the patient has less than ten years to live, most doctors will not recommend a prostatectomy. Instead if the patient is elderly or in poor health he may be given Hormone Therapy. He may also be offered other forms of treatment that are not quite as traumatic as radical surgery such as Cryosurgery, Brachytherapy or Seed Implants, External Beam Radiation (XBRT), or Proton Beam irradiation. For advanced disease, the patient may be offered various forms of chemotherapy.

You should always remember though, no matter what the doctor recommends, it is your body, your disease and your choice of treatments. Of course, you should take into consideration that the doctor should know more than you do. But if you ask ten doctors what the best treatment would be, you may get ten different answers. You must endeavor to learn all you can, then make your own decision.

In Greek mythology, Aphrodite, the goddess of beauty and love, sprang fully grown and mature at birth. Unlike Aphrodite, cancer starts from a single cell and grows. Your cancer is not going to kill you overnight. It may have taken 10 years or more to become significant enough to be detected. You have a bit of time to do your study. Don't let anyone rush you into a treatment that you may regret later. A very important part of your decision is choosing the best doctor.

Cancer is not Contagious

Cancer may cause some people to avoid or shun a cancer victim or to be afraid of them. But cancer is not contagious. It cannot be transmitted to another person. Cancer is nothing more than a few of the body's own cells that have begun to multiply abnormally. Cancer can only derive from the cells in your body.

Cancer and Pain

Some cancers can be terribly painful, disabling and traumatic, not only to the person who has it, but to the whole family. If a close friend or relative is suffering, you may also suffer right along with them.

If the cancer is causing a lot of pain, there are several things that a doctor can do to alleviate the pain. Sometimes radiation will help. Sometimes it may be necessary to use morphine and other strong pain killers. Often metastatic prostate cancer spreads to the bones and causes great pain. A radioactive isotope strontium 89 can often relieve the pain. Some chemotherapy drugs are good at relieving pain caused by metastases. More about chemotherapy in Chapter 15.

There are some cancers that cause no pain or alarm at all until they have spread and metastasized. Since they cause no pain or alarm to the body, it is often difficult to find them before it is too late to properly treat them.

Some Cancer Signs
Here are some signs that should cause suspicion of cancer in men, women or children: Any increased skin pigmentation, a sore that does not heal, unusual bleeding, a thickening or a lump in the breast or anywhere in the body, indigestion or difficulty in swallowing, rectal bleeding, a change in the bowel habits that persists, shortness of breath, fatigue, change in a wart or mole, bone pain, frequent urination, and decreased urinary stream.

Having one or more of these symptoms does not necessarily mean that you have cancer. Or you may have none of the above symptoms and still have cancer. It can be a silent killer. But it is very easy to get checked out. We will say it again and again. If the cancer is found early enough, it can be cured. The answer to cancer is early detection.

Cancer And You
It appears that some prostate cancers may be caused by some environmental factors and perhaps diet. A recent study done by Dr. Edward Giovannucci at Harvard Medical School seems to indicate that fats from red meats are a contributing factor in prostate cancer. Animal fats are also highly suspect as a factor in breast cancer development.

In Japan clinical stage prostate cancer is very low. But if they come to the United States, their rate is about the same as for Caucasians. When autopsies are done on Japanese men in Japan they find about the same rate of undetected prostate cancer as that of American men. Because of the crowded conditions in Japan, they have very little land on which to grow cattle. Most meat is imported and is very expensive. So most families eat very little meat. Instead they eat a lot of fish and soy products.

We do know that there is one thing that does not cause prostate cancer. That is sex. Even overindulgence in sex acts of any kind or masturbation does not cause prostate cancer. This is one area where you can’t get too much of a good thing.

Causes of death
Ordinarily, cancer cells alone do not cause death. The body is a fantastic machine. It is also very adaptable and can survive and overcome unbelievable traumas and injuries.

Unless the cancer destroys a vital organ such as the brain, lungs or heart, it does not directly kill the host. It may kill by cachexia (kakos is Greek for bad, hexis means condition). Cachexia is a state of ill health, malnutrition and wasting.

Many cancer patients lose their appetite which causes malnutrition. It appears that the tumors may produce factors that cause cachexia.

When prostate and breast cancers metastasize, the cells often set up new colonies in the bones of the vertebrae. The bones may become eroded. The calcium from the eroded bones may be taken up by the blood stream. The body must have a certain amount of calcium. But if there is too much in the blood stream, it may cause hypercalcemia.

Hypercalcemia may cause a change in mental alertness, anorexia, nausea, vomiting, constipation, excessive thirst, frequent urination, muscle weakness and a diminished muscle reflex. Kidney failure is common. Hypercalcemia is very serious and is associated with a high mortality rate. Prostate cancer may also cause blood coagulation problems and anemia.

In an old classic textbook, a fifth edition of Boyd's Textbook of Pathology, published in 1947 by Lea & Febiger, Philadelphia. The following is quoted from this book, page 14:
"... disease is not a state; it is rather a process ever changing in its manifestations, a process which may end in recovery or in death, which may be acute and fulminating in its manifestations, or which may represent the slow ageing of the tissues brought about by the sharp tooth of time. ...(a) lesion (may have) been present during many years of life, and its presence is not sufficient to explain the final end. ...the pathologist has to try to explain not only why the patient died but how he was able to live". As Boycott remarks (Lancet, 1933, 2, 846) "I do not wonder that people die; that is easy enough. What I marvel at is that they go on living with bodies so maimed, so disordered and worn out"".

One factor that makes prostate cancer so life threatening is that it affects mostly older men. The "sharp tooth" of time has dulled and weakened their normal body defenses. Thus they may be more susceptible, and less immune, to the many lesser infections and opportunistic diseases.