An Oncologist's View of Prostate Cancer:

Understanding the Facts, Sorting through the Options

2nd Edition

by Srinivasan Vijayakumar, MD, DMRT, FACR

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Dedicated to:

Thatha and Patti
&
Appa and Amma

Srinivasan Vijayakumar, MD, DMRT, FACR

Foreword

To the reader,

Claire Pomeroy,
Professor,
Vice Chancellor
and Dean
School of Medicine
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Prostate cancer is the second leading cause of cancer death among men in the United States. One in six American men will be diagnosed with prostate cancer. For the men who are diagnosed, for their families and friends, this disease has an impact that goes far beyond the statistics. The angst of a serious illness, the struggle to choose the best therapy, and the lifestyle adjustments to the side effects of surgical and medical treatments all exact a toll on men throughout our community. Every day, patients display great bravery and strength in their fight for health and dedicated clinicians and researchers work to bring caring, comfort and new hope for the future.

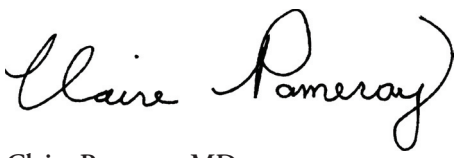
All men must be aware of their risk for prostate cancer. Let's work together to spread a message about the importance of screening. And for those of you who have already been diagnosed, I urge you to form a partnership with your physician and work together to choose the best treatment, with particular emphasis on close and diligent follow-up. As you make the brave and challenging journey of dealing with your cancer, open communication and trust are essential.

We now know that there are significant disparities in the incidence and outcomes of prostate cancer. For example, black men have a 50% greater chance than white men of getting this disease and black men are twice as likely to die of prostate cancer compared to whites in the United States. We urgently need to better understand these disparities and to work to ensure that all patients have affordable access to early diagnostic services and state-of-the-art treatment options.

Many questions remain about the best approaches to treatment for prostate cancer. When is surgery indicated and when is "watchful waiting" better? What about radiation therapy and hormonal therapy? For now, no one option is right for everyone and each patient should talk with his physician about the best approach for his individual case. Many talented researchers are dedicated to finding the an-

swers to these questions, providing great hope for the future in our quest to conquer prostate cancer.

This book is a wonderful step toward achieving the goal of improved understanding of prostate cancer. It will prove invaluable for patients and their loved ones. Dr. Vijayakumar builds on his many years of experience in the field of radiation oncology to provide practical insights for patients embarking on their fight against prostate cancer. Together with an expert group of contributors, Dr. Vijayakumar provides the advice that patients and their families need, so that they can partner with their physicians to assure the best possible outcomes.



Claire Pomeroy, MD
Professor
Vice Chancellor and Dean
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Foreword

To the reader,

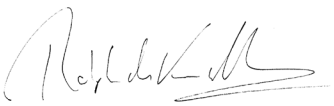
Ralph W. de Vere White
Director,
UC Davis Cancer Center

As we get older we all fear that one day we are going to hear those dreaded words that we have cancer. One of the problems of being a man and growing older is that your chance of hearing those words is very considerable. Close to 300,000 men this year in America will have heard those words. At that time there are two things to bear in mind. The first is that luckily, for the vast majority of people, the outlook will be excellent. The second is that you want to find a reliable source of information that will allow you to successfully undertake what may be a long journey.

In putting together the team that will look after you, key will be your doctors, nurses and other health care providers. However, an informed patient can greatly help this team. An informed patient is much more likely to make the right decision. In this case there may be multiple correct decisions; the right one is the one that suits your particular circumstances best.

Today many men, when told they have prostate cancer, will turn to the Internet. While it can be a source of much information, there is no great filter to tell you what is correct. In the present book, Dr. Vijayakumar and his colleagues have put together an extraordinarily readable, very well laid out, and very balanced account of what prostate cancer means, the value of screening, what happens if your PSA is elevated, what choices can be made when you have reached a diagnosis, the pros and cons of these choices, and your expected outcome.

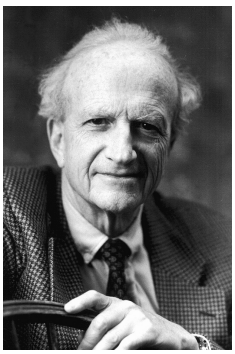
Finally, many men will go through the journey of prostate cancer with a partner. On many occasions the worries and fears are equal, if not greater, for the partner than for the patient. This book will provide an excellent and very reassuring source of information for the patient, his partner and family.



Ralph W. de Vere White, M.D.
Director
UC Davis Cancer Center

Foreword: *A Patient's Perspective*
(From 1st Edition)

To the reader,



Gary S. Becker,
Professor,
University of Chicago

In the winter of 1994 I decided to have a PSA test because a close friend was dying of prostate cancer. I had no symptoms and a physical exam revealed no evidence of any problem. Yet, to my surprise, I discovered that I had a very elevated reading. A short time later a biopsy revealed evidence of significant tumor growth.

I was 63 years old, and was devastated by the news. Like most men, I was not well-informed about the biological role of the prostate. Even worse, I was completely ignorant of the possible treatments and prognosis for someone of my age who develops this form of cancer. I consulted several urologists and surgeons in the Chicago area, read a little of the technical literature, and called one or two knowledgeable friends. But I was too dazed by the news to analyze the information very clearly.

I learned that surgical removal of the prostate was one option; another option was to do nothing (so-called "watchful waiting"); and that radiation treatment was a third option. Unfortunately, there is no magic bullet that provides a certain cure for this cancer, but the prognosis is very good when it is detected early and if a reasonable choice is made among possible treatments. Doing "nothing" may be the best treatment for some older men, but for most men the prognosis appears to be better with more aggressive action. Unfortunately, the data are less conclusive than one would like.

I decided on the aggressive approach of what is called nerve-sparing prostatectomy, which is surgical removal of the prostate that tries to do minimal damage to surrounding nerves. I was fortunate to have a fine surgeon at the University of Chicago Hospitals, Dr. Charles Brendler.

In retrospect, I believe that I chose a good option for me, given my age, tumor quality and other factors. Still, I would have benefited greatly from having access to a clearly written, non-terrifying book that discussed in simple language the advantages and disadvantages of various treatments. Dr. Vijayakumar has now written such a book. Since he shows in Chapter 1 that the chances of men developing prostate cancer increase after age 50, this book should be extremely helpful to all middle-aged and older men.

Dr. Vijayakumar's book contains chapters on all the reasonable options, including surgery to remove the prostate, various types of radiation therapy, hormonal therapy, and watchful waiting. He also discusses newer and more experimental approaches. As a radia-

tion oncologist he tends to favor radiation, but he objectively presents the strengths and weaknesses of all approaches, including those most competitive to radiation. Moreover, he does this in simple language that does not require detailed medical and biological knowledge.

Anyone who learns that he has cancer of the prostate would be helped by knowing about the options available before making the very difficult choice of treatments. This does not mean that a patient should try to act as his own doctor, for that is neither feasible nor advisable. But, since different physicians advocate different approaches, and there is some competition among these approaches, an informed patient can better judge the advice he receives.

In my case, surgery helped out but, unfortunately, did not provide a cure. So, I had to look for additional forms of treatment. I did not have access to Dr. Vijayakumar's book, but I did have access to him and others who provided me with excellent information about the options available. Two-and-a-half years after the surgery I decided to have a version of conformal radiation therapy treatments combined with hormonal therapy (a treatment discussed in Chapter 6 of this book). I am indebted to Dr. Vijayakumar and Dr. Samuel Hellman (at the University of Chicago Hospitals) for their excellent care and attention.

I believe that during the next 10-20 years, major progress will be made toward discovering a real cure for most prostate cancers. But until then, one has to try to use the best treatments available in the most effective ways. I strongly recommend this book for anyone who wants to learn in a patient-friendly way about the several reasonable options presently available to the many men who will learn that they have prostate cancer. Learning that you have prostate cancer is bad news, but it will be less terrifying after reading this valuable book.

Gary S. Becker
Professor
Departments of Economics and Sociology
University of Chicago
Nobel Laureate

Foreword: *Increasing Public Awareness about Prostate Cancer*

(From 1st Edition)

To the reader,

John H. Stroger, Jr.,
President,
Cook County Board
of Commisioners (IL)

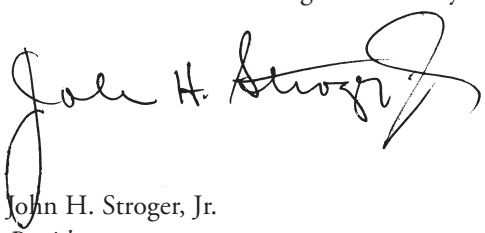
As one of thousands of prostate cancer patients and survivors, I am humbled at the opportunity to acknowledge this book as a tool for all men who find themselves faced with the difficult and complicated decisions associated with prostate cancer.

And as an African-American man, I find myself motivated to encourage other African-Americans to make sure they are properly educated and screened for the early detection of prostate cancer. This relatively unknown and unrecognized disease disproportionately affects African-Americans. In fact, African-Americans represent about 18% of the diagnosed cases in the United States each year.

Although I had been screened for prostate cancer before, I had always dismissed the screening as a routine test and something I could forget about after leaving the doctor's office. In 1994, I could no longer dismiss that premise when, after one of those routine screenings, I was faced with an elevated level of prostate specific antigen indicating the likelihood of prostate cancer. Upon notification of my test results, I contacted friends who had been faced with this same situation to get a better idea of what I could expect in the months to follow. Then I took some time to contact several doctors to get their advice. This is how I found Dr. Srinivasan Vijayakumar. His approach to my situation was just right for my family and me, and this book is just right for other victims and their families.

I encourage all men and their families to use this book as an educational tool during their experience with prostate cancer. It can relieve a lot of the stress you will find yourself faced with and answer most, if not all of your questions. It will put to rest some of your fears, educate you about treatment options and prepare you for dealing with prostate cancer.

Finally, I would like to thank Dr. Vijay for his compassionate treatment and sensitivity. His ongoing commitment to educating men and their families about prostate cancer both inside and outside his medical office further exemplify his dedication to the health and well-being of men everywhere.



John H. Stroger, Jr.
President
Cook County Board of Commissioners (Illinois)

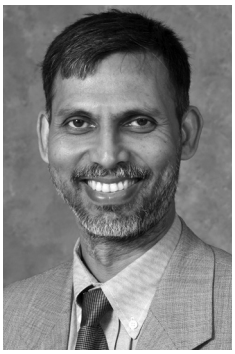
A special note to African-American men: African-American men have the highest rate of prostate cancer in the world and have a more advanced cancer when diagnosed. Because of this, it is especially important to raise awareness about prostate cancer among the African-American population, and to educate about early detection of prostate cancer through digital rectal exam and PSA testing. When cancer is detected at an early stage, the patient has the best chance to be cured.

Introduction

Prostate cancer is the most common form of cancer affecting men. Yet, until recently, little had been written about prostate cancer or benign diseases of the prostate, and men rarely discussed it with their colleagues, even though most men will experience some sort of problem with their prostate in their old age. In the 1990s, however, prostate cancer caught the attention of the American public, resulting in an abundance of information. While plentiful, the information is sometimes confusing or conflicting.

This book attempts to sort through the information and present the facts about prostate cancer in a clear manner, to help the man with prostate cancer make a well-considered decision about the course of treatment. The book is meant as a tool to supplement – not to replace – discussion between you and your physician.

This book is written from the perspective of a cancer specialist. I have been an oncologist for more than 20 years, specializing in treating cancers of the prostate and lung.



Srinivasan Vijayakumar, M.D. ("Dr. Vijay")
Professor and Chair,
Department of Radiation Oncology
UC Davis Cancer Center

Who is this book for?

This book is primarily for men who have early stage prostate cancer and are deciding their first treatments. It is also written for non-oncologist physicians and other health professionals. While I cover some treatment choices for advanced cancer, that is not the main focus of this book. Family members of men with newly diagnosed prostate cancer should also read this book to increase their understanding of what men have to consider, and will go through, as they begin their treatment.

Treatments for prostate cancer have improved considerably and you should be quite hopeful as you think about how to deal with your prostate cancer. If you have caught the disease in its early stages, you have an excellent chance of being cured; and if that is not possible, of living well with it. Newer treatments are minimizing side effects and you will learn strategies to cope with cancer. You and your families undoubtedly have many questions and fears about prostate cancer. I urge you to start asking questions during your first few visits, before deciding on treatments. You have to ask the questions – no one will do it for you. If you take an active role in your care, chances are you will cope better with your cancer. You can't avoid this disease by never bringing it up. Talk to many people, read avidly, and then take a break and make a positive plan. Over time, you will adjust to your diagnosis and gather courage within you. As you understand more about the disease your fears will lessen and you will focus on the next steps you need to take to cure or manage your cancer.

Take Time to Make the Best Decision for You

Often, when a diagnosis of prostate cancer is made, patients and their families and friends are faced with a sudden, overwhelming avalanche of verbal information about the prostate gland, prostate cancer and treatment options. The patient and his loved ones must confront uncomfortable concerns:

- A sudden and uncertain diagnosis of cancer...the dreaded "C" word.
- A problem that is located in a sexual organ, with its associated additional anxieties and difficult-to-discuss feelings.
- Feelings of guilt.

Some men may wonder if they have prostate cancer because of something they've been eating; because of too much or too little sex; because of a one-night stand or adulterous affair, or because of other unrelated circumstances (none of these are true, for we do not know what causes prostate cancer). They may experience:

- A confusing litany of treatment options and, perhaps, contradicting opinions from different physicians.
- Too much information in too little time. Numerous resources – books, booklets, videos, Internet web pages – can answer many of the questions that arise in the man newly diagnosed with prostate cancer, and among his family and friends.

Why read this book?

This book is designed to explain the many aspects of diagnosing and treating prostate cancer...in layman terms that are easy to understand. Much of this is based on actual questions posed by patients. This book also discusses some of the new developments – such as neoadjuvant hormonal therapy and intensity modulated radiation therapy – that are not well discussed in literature available for the general public.

This is my attempt to explain things in my own way. I hope these explanations will make it easier for you and your family to understand the complex issues involved and to make rational decisions that meet your specific needs.

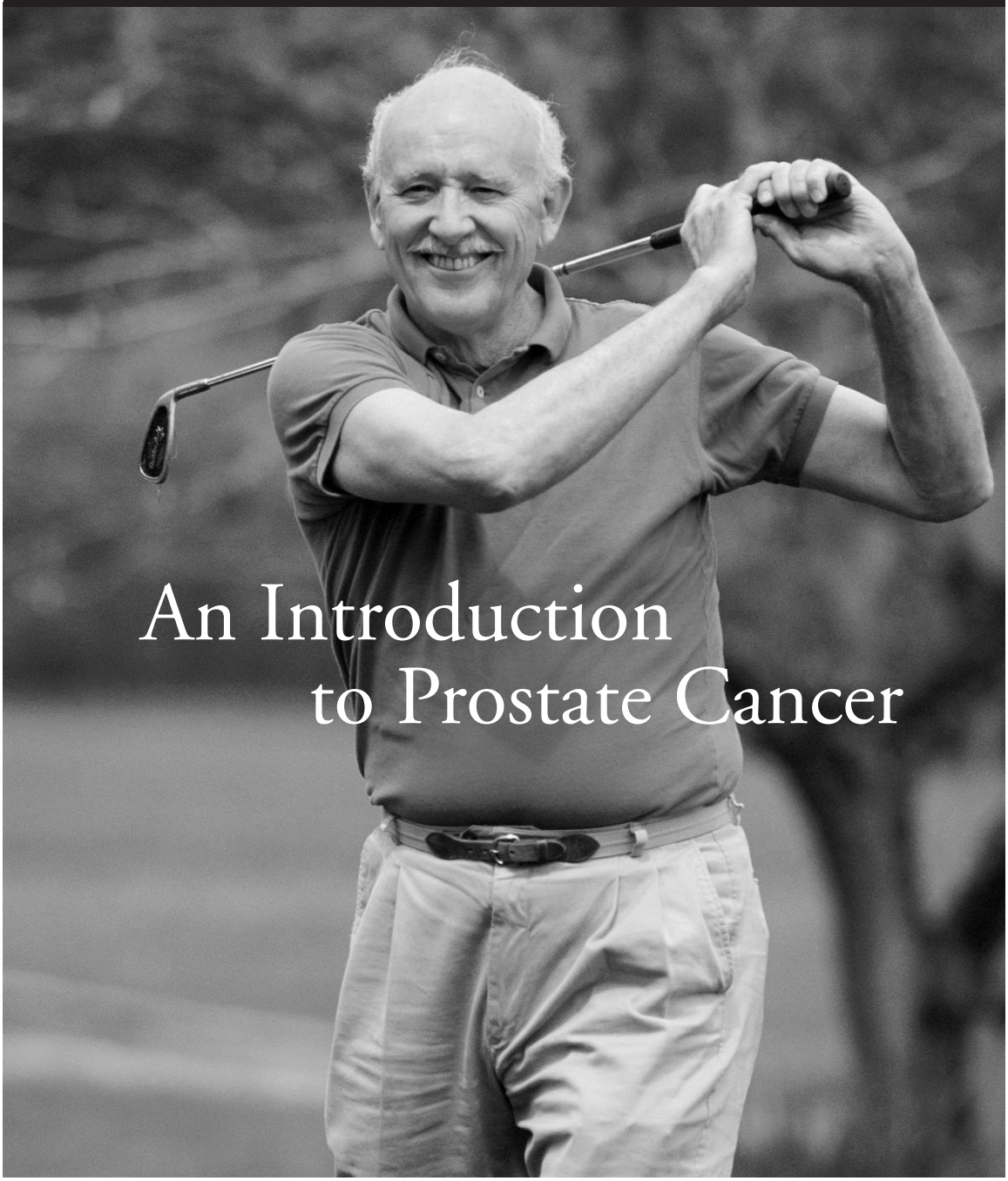
This book also incorporates information on many new advances that have occurred in the past few years, based on new scientific evidence.

Finally, this book strives to convey complex topics and scientific concepts in a simple, easy-to-understand format that makes the subject interesting and informative. Use it as a tool in your treatment decision process.

Srinivasan Vijayakumar, MD, DMRT, FACR ("Dr. Vijay")
Professor and Chair
Department of Radiation Oncology
UC Davis Cancer Center

Contents

Chapter 1



An Introduction to Prostate Cancer

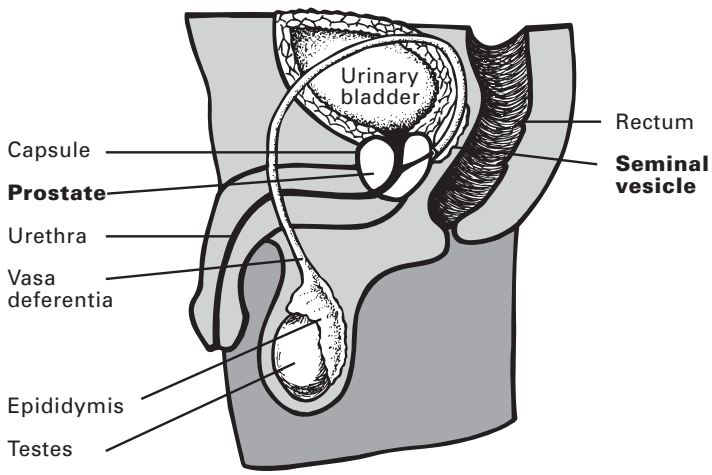
It's important to understand a few general concepts about prostate cancer. Some of these points will be discussed in more detail later in this book.

What is the prostate, and what does it do?

The prostate is a small gland, found only in men, that produces a white fluid. This fluid is one part of semen, containing sperm. Before puberty, the prostate is about as small as an almond. At puberty, the prostate gland doubles in size, to about the size of a walnut. Then, around age 45, a man's prostate may begin to grow again and may continue growing for the rest of his life. This growth is normal and does not indicate cancer; it is called benign prostatic hyperplasia (BPH). The prostate gland is located just below the bladder and in front of the rectum. The prostate gland actually wraps around the urethra–the tube that carries urine and semen through the penis and out of the body. As the prostate grows, it sometimes presses on the urethra and can interfere with urine flow [Figure 1]. Because of its location, problems with the prostate, such as cancer, BPH, or prostatitis (inflammation of the prostate gland), affect both the reproductive and urinary systems.

The prostate has two lobes, right and left, and can be divided into five zones, two of which are the "transition zone" and the "peripheral zone". The transition zone is located in the central part of the prostate and this is where the benign growth occurs in many men that leads to the development of BPH in most men by the time they are 80. The peripheral zone, which is horseshoe-shaped, is found next to the rectum, on both sides of the urethra, and is where most prostate cancer develops.

Figure 1



The principal male hormone, testosterone, which is produced in the testes, affects the prostate's growth and function. This has implications for the treatment of advanced prostate cancer.

What is cancer?

Cancer is an unwanted growth in the body. This growth (a malignant tumor) is made up of millions of microscopic cells: cancer cells. There are a few unique characteristics of cancer cells, but the most important is that they keep growing and growing. In other words, the body has no control over these villains. In time, cancer cells will "metastasize" by invading other parts of the body.

Cancer cells are genetically coded for your body (which is why you can't infect another person with cancer). Each cell in your body has DNA (deoxyribonucleic acid), which provides a blueprint for the growth and functioning of that cell. When cells divide, the genetic code is copied. When something goes wrong with the DNA, malformed cells develop and reproduce uncontrollably. Usually your body eliminates damaged cells, but when it is unable to, cancer can develop. Cancer cells can form 'tumors,' which are abnormal growths, and can be malignant (cancerous) or benign (non-cancerous). As with many cancers, we do not know what causes prostate cancer to develop.

How does cancer spread (metastasize)?

Almost all cancers can spread from one part of the body to another. The spread can occur in three different ways:

- Cancer can invade tissues in the immediate vicinity, close to the primary tumor.
- Cancer cells can get into the blood and spread to distant parts of the body. For example, they can spread from the prostate gland to the bones or lungs.
- Cancer can track along tiny lymph vessels to lymph nodes located throughout the body. Lymph is a mostly clear fluid that contains white blood cells and drains waste from cells, including cancer cells. This fluid travels through lymphatic vessels and into lymph nodes. When there are too many cancer cells, the lymph nodes cannot remove them all.
- Cancer cells can also "travel" in the lymphatics.

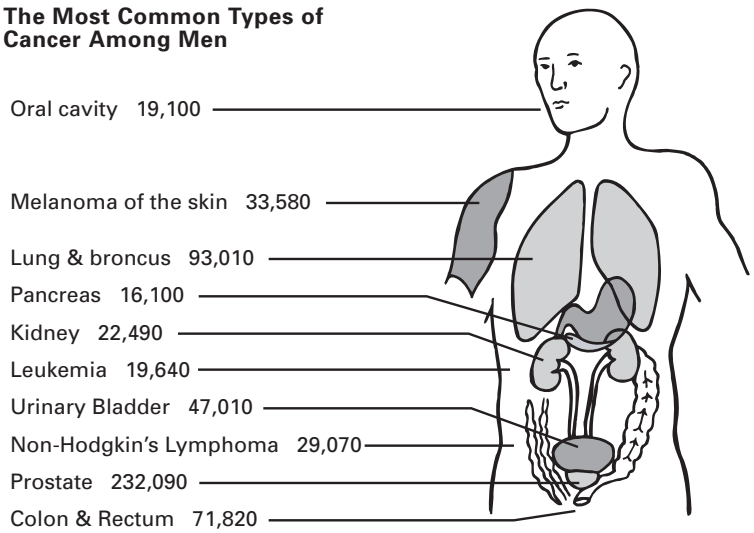
In prostate cancer, if the cancer is still confined to the prostate gland, it is considered an "early stage" cancer. (See Chapter 3 for more on stages.)

Almost all prostate cancers develop inside the prostate gland (making it an "adenocarcinoma") and grow slowly within the gland, but left untreated they can eventually metastasize to other tissue, organs and bones (especially in the hip and lower back). Prostate cancer may first metastasize to the lymph nodes in the pelvis. If given time to develop, prostate cancer becomes more aggressive and faster growing, and learns to adapt to environments outside of the prostate, and reaches a point where it is no longer curable. Prostate cancer is "multifocal," meaning that it appears at several spots in the prostate simultaneously, so treatments for prostate cancer must treat the whole prostate (usually, radiating it, or removing it in surgery).

What is the "incidence" of prostate cancer?

"Incidence" refers to the number of men in a random group of 100,000 living men who will have the disease. Incidence is often expressed for a specific geographical region: a city, a state, or a country, or for a specific age category. In the United States, the incidence of prostate cancer for men of all ages is 160 per 100,000 men. The American Cancer Society estimated about 232,000 new cases of prostate cancer in the United States in 2005. The next most prevalent cancer was lung cancer, with an estimated 93,010 new cases in 2005. [Figure 2]

Figure 2 **The Most Common Types of Cancer Among Men**



[1]Cancer Facts & Figures 2005, *American Cancer Society, Inc. (With permission.)*

Table 1. Estimated number of new cancer cases in US males (1997-2005)

Year	All Cancers	Prostate Cancer
1997	785,200	334,500
1998	627,900	184,500
1999	623,800	179,300
2000	619,700	180,400
2001	643,000	198,100
2002	637,500	189,000
2003	675,300	220,900
2004	699,560	230,110
2005	710,040	232,090

Source: American Cancer Society's Cancer Facts & Figures - 1997-2005.

What do we know about the incidence of prostate cancer in American men?

- Prostate cancer is the most common form of cancer in American men, and strikes men about as often as breast cancer strikes women.
- Prostate cancer is most prevalent in men over age 65 and is fairly common in men 50-64. However, prostate cancer can strike men younger than 50.
- The incidence (number of cases) of diagnosed prostate cancer among American men has been increasing in recent years. The incidence has risen in recent years, after declining slightly since the mid-1990's. In part, this is due to improved tests that detect prostate cancer earlier.
- While age is the greatest risk factor for prostate cancer, two other major risk factors are race and family history. Incidence of prostate cancer is higher among African-American men than Caucasian men, and higher among Caucasians than Asian-Americans. African-American men also get more severe forms of prostate cancer, and are more likely to die from prostate cancer than men of other races in the United States, perhaps because the disease is often more advanced in them when it is first detected. This underscores the importance of early detection of prostate cancer in African-Americans, and indeed in all men. Cancer that is detected early can be cured.
- First-generation immigrants tend to have an incidence of cancer similar to that of the country of their birth; but by the second or third generation, the incidence of prostate cancer catches up with the general American male public, suggesting that environment and diet may influence who gets prostate cancer.
- Men with a family member who has had prostate cancer are at higher risk than

other men. Men with a father who had prostate cancer have twice the risk of developing the disease; if a father and a brother had it, their risk is tripled. Those with three relatives with the disease, or with two relatives who developed the disease before age 55, are at even higher risk of getting prostate cancer. *Please remember that these are statistics about risks—not statements of certainty about who will actually develop prostate cancer.*

Why has the incidence of prostate cancer gone up in recent years?

Most experts believe that the true incidence of prostate cancer has risen, but are uncertain about the reason. However, there are a number of factors that contribute to the rise in reported "incidence."

- The incidence of prostate cancer naturally increases with age [Table 1]. Because men (and women) are living longer now than even two decades ago, and because the risk of prostate cancer increases with advanced age, the number of men being diagnosed with prostate cancer has increased.
- Because physicians and the lay public have become more aware of prostate cancer in recent years, we may be diagnosing more and more "latent" cancers.
- With the use of the blood test for prostate specific antigen (PSA), doctors are detecting more prostate cancers than before. (See Chapter 2 for more on PSA.)
- Men over 70 are more likely to have prostate cancer because men in general are living longer and the PSA test detects prostate cancer in its earliest stages.

Table 2

Age Group	Chances of Developing Prostate Cancer
Lifetime risk	1 in 6
Birth to 39 years	1 in 10,000
40 to 59 years	1 in 103
60 to 79 years	1 in 8

Table 3: Estimated New Cases of Prostate Cancer, and Deaths, by Year

Year	Estimated New Cases	Deaths
2005	232,090	30,350
2004	230,110	29,900
2003	220,900	28,900
2002	189,000	30,200
2001	198,100	31,500
2000	180,400	31,900
1999	179,300	37,000
1998	184,500	39,200
1997	334,500	41,800
1996	317,000	41,400
1995	244,000	40,400

Source: American Cancer Society's Cancer Facts & Figures - 1995-2005.

How does prostate cancer compare with other types of cancer?

There are many different types of cancer. Each cancer has unique characteristics, acts in its own manner, and has its own rate of cure vs. mortality (death rate). For example, Hodgkin's disease (a cancer of the lymph system) has a very good cure rate. Cancer of the pancreas, however, has a very poor cure rate and high mortality. The good news is that, in general, prostate cancer patients have about 6-8 times better odds of beating the cancer and living for 5, 10 or 15 years after the diagnosis and treatment of cancer has been made than do patients with cancers of the lung or esophagus. In fact, prostate cancer has a better survival rate than cancers of the pancreas, kidney, brain, and other organs. And, many more patients with prostate cancer have healthy characteristics that favor their results, compared to lung or esophagus cancer patients. (For example, most lung cancers are related to smoking, which seriously impairs health.) The bottom line is that many men tackle prostate cancer and live many years after their diagnosis and treatment. Nonetheless, because it strikes so many men, prostate cancer still is the second leading cause of cancer deaths among men in the U.S.

What are latent cancers?

Like any cancer, a latent cancer continues to grow uncontrolled. However, a latent cancer typically grows too slowly to "kill" its host as a more aggressive cancer can. A man with a latent prostate cancer will die of something else, such as a heart attack, before the cancer would kill him. In many cases, the man did not even know he had cancer, and cancer was only discovered when the prostate gland was examined after his death. In a case like this, the heart attack was the cause of death, prostate cancer was not. So, the man's cancer had been "latent." The man died with prostate cancer, but not from prostate cancer. Some prostate cancers tend to be aggressive; others are more docile or dormant. In autopsy studies of men who died of something other than prostate cancer, 15-30% of those older than 50 years will harbor prostate cancer. Of men older than 80 years, 60-70% will have cancer in their prostate. These men died with prostate cancer, not from prostate cancer. A "latent cancer" is one that would not have been diagnosed in a man except for the new tests, such as the PSA blood test.

Latent cancer will not kill a man; he will die of something else first. Latent cancer will not spread. Latent cancers don't require treatment.

How would a man know that his prostate cancer is "latent" and probably will not kill him?

That is a tough question, but a good one. There are no tests that can tell us decisively which prostate cancers are latent. In any man with prostate cancer, we cannot determine with certainty whether that man has a "true" cancer or a "latent" cancer. However, in medical lingo, doctors call some cancers "insignificant." One commonly used definition of an insignificant cancer is: a prostate cancer that is less than 0.5 cc (cubic centimeters) in size.

How can you tell if a cancerous tumor is small or latent?

Without surgically removing the prostate, nobody can determine the size of a tumor with any certainty. However, there are certain factors that indicate the likelihood of a prostate cancer diagnosed in a man being medically "insignificant." The following self-test can determine the likelihood that your cancer is small and not life-threatening. Keep in mind that this provides only a general sense of your risk factors; sophisticated diagnostic tests provide a more accurate perspective on your specific cancer.

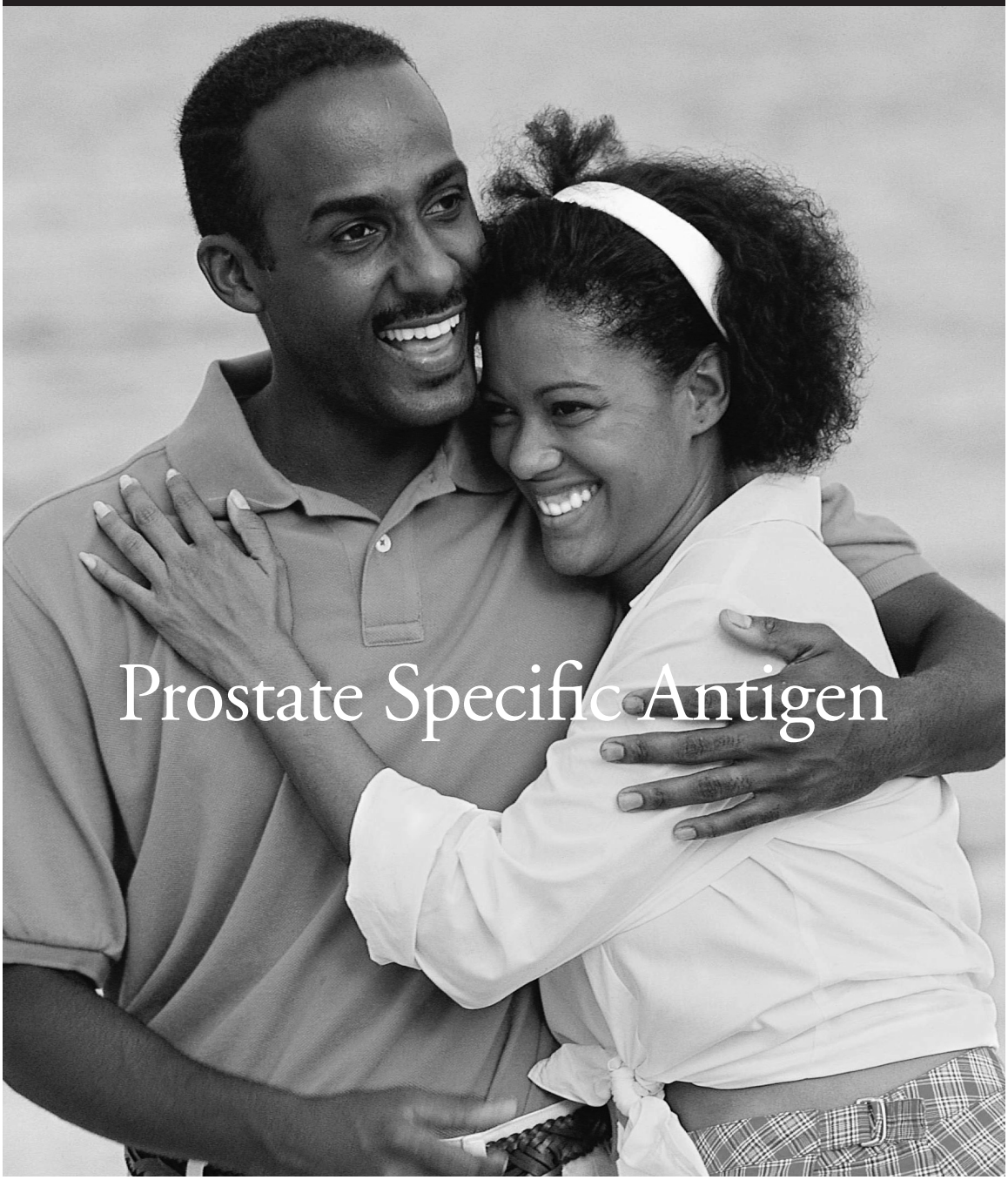
Test

1. I was older than 72 years when cancer was found.	☐ **Yes**	☐ **No**
2. My doctor did not feel any cancer nodules in my prostate nor did the doctor suspect cancer when examining my prostate.	☐ **Yes**	☐ **No**
3. My cancer is well differentiated; or the Gleason score is 2-4; or my cancer is so small that no grade could be assigned. (See Chapter 3 for more on Gleason scoring and grades.)	☐ **Yes**	☐ **No**
4. My PSA is less than 4. (If my PSA is more than 4, my PSA density is less than 0.1.)	☐ **Yes**	☐ **No**

If your answers to Questions 1-4 are all "Yes," then it is very likely that you have a "latent" or "insignificant" cancer. However, before you decide that you have an insignificant cancer and don't need treatment, talk to your doctor. Only a doctor can scientifically determine whether it is insignificant (latent).

The concept of "latent" cancer is controversial. The discussion here is mainly to explain concepts to you.

Chapter 2



Prostate Specific Antigen

Prostate specific antigen (PSA) is a protein molecule found in the semen. It also leaks into the blood, and can be found through a blood test. Made in the prostate, the function of PSA is to help sperm swim after ejaculation. Some PSA in the blood floats freely ("free PSA"). However, most PSA in the blood is attached to another protein and therefore not free ("complexed PSA"). PSA exists in moderate amounts in healthy men without cancer. However, an elevated level of PSA can indicate the presence of prostate cancer (elevated PSA can also indicate non-cancerous conditions, such as BPH [benign prostatic hyperplasia], an infection, or inflammation). Prostate cancer cells produce about 10 times more PSA than healthy non-cancerous cells and this makes PSA a useful tumor marker for prostate cancer.

The Basics on PSA

- PSA stands for "prostate specific antigen."
- PSA is a protein, secreted by the prostate gland but also found in small amounts in the blood.
- PSA is secreted by both normal and cancerous prostate tissue. Cancerous cells secrete about 10 times more PSA than normal prostate cells.
- Normal PSA blood level is 0-4 nanograms per milliliter (ng/ml).
- A man with prostate cancer can have a normal PSA level, but generally, the chance of having prostate cancer increases when PSA values are above 4 ng/ml. Because about 25% of men with prostate cancer will have a low PSA, health experts recommend having a DRE with the PSA test.

What is the "normal" level for PSA?

A PSA level ranging from 0 to 4 is considered normal in men (meaning 0-4 nanograms [billionths of a gram] per milliliter of blood). However, PSA values generally increase with age, so some physicians consider an age-adjusted PSA value. As men age, their prostates become larger, and many develop BPH, which elevates PSA. Therefore, PSA will vary with a man's age. This generally leaves 4 as the maximum level for men in their sixties, and lower figures for younger men.

Can the size of the prostate gland affect the PSA level?

Yes. After age 45, the prostate tends to grow, and a larger prostate gland will naturally produce more PSA. Therefore, your doctor should determine the size of your prostate when evaluating your PSA level. PSA density is the level of blood PSA, adjusted for the size of the prostate gland (this can be determined by transrectal ultrasound). A high PSA density indicates a greater chance of having prostate cancer.

How is PSA measured?

PSA is measured through a blood test called an "assay." There are different types of assays which measure PSA slightly differently. So, it's important to know the type of assay that is being used to evaluate PSA level. (In essence, an assay is a different brand-version of the PSA blood test.) PSA level must be considered against such factors as a man's age, the size of his prostate gland, and the type of assay being used.

Is the PSA test new, and what does it do?

PSA testing has been widely used at many academic medical centers since the Food and Drug Administration approved it in 1986. PSA level is measured by taking a small sample of blood and analyzing it for PSA.

The PSA test has many uses:

- PSA can detect prostate cancer early. If the PSA is above 4 ng/ml, your doctor will probably recommend a biopsy to find out whether or not you have cancer.
- PSA can help predict the likelihood of recovery in men who have prostate cancer. If the PSA is high, there is a greater likelihood of the cancer having spread beyond the prostate, which makes cure less likely.
- PSA can be used to determine what further tests are necessary, when they are combined with your Gleason score and your doctor's clinical examination.
- PSA can indicate whether or not the cancer has been cured after treatment, as rising PSA can be an early sign that the treatment was not effective.

PSA testing has been a huge advance in the battle against prostate cancer because with it men can have their prostate cancer detected in its early stages, when it is still confined to the prostate and is therefore curable. Prostate cancer does not usually cause symptoms in its early stages, when it is easiest to treat, so only the PSA test (with DRE) can detect it.

However, the PSA test is not perfect. A high PSA can be caused by an enlarged prostate, inflammation of the prostate, infection of the prostate, or older age, and so it does not necessarily indicate cancer. Also, not all prostate cancers need to be treated, and doctors cannot tell which cancers are most likely to spread and which ones are benign. Also, a normal PSA test may miss some prostate cancers.

What does the PSA level indicate?

PSA level can suggest the presence or absence of prostate cancer. If you have a high PSA, to determine if you have cancer your doctor may recommend a biopsy of the prostate, since PSA level alone cannot tell you if you have cancer. PSA itself is not the cancer. Think of PSA like a fever in someone with pneumonia. The pneumonia – not the fever – is what makes the person sick. The fever –100° vs. 104° – helps indicate how sick that person may be from the pneumonia.

In general:

- Larger cancer = higher blood PSA value.
- More advanced cancer = higher blood PSA value.
- Lower blood PSA value suggests better chance to respond to cancer treatment.

PSA has been found in other tissues, including breast tissue; however, PSA exists in very minute quantities in these other tissues.

If your PSA level is greater than 10 ng/mL, your doctor may suggest a biopsy. PSA results between 4 and 10 ng/mL are borderline and can lead to further testing or suggest other prostate conditions, such as BPH or prostatitis. However, some men have high PSA levels and have healthy prostates. A high PSA level does not necessarily indicate prostate cancer, just as a normal PSA level does not absolutely mean a man does not have cancer. One additional test is a transrectal ultrasound (TRUS), which identifies abnormal areas of the prostate that require a biopsy (however, TRUS may not see all the cancers, so do not rely on just this test for any treatment decision).

Can PSA blood values go beyond the normal range temporarily and return to normal?

Yes, after an infection in the prostate or bladder, or after bladder catheterization. Usually it decreases to the normal range after the infection is treated with antibiotics. After a biopsy of the prostate gland, the PSA value can be elevated. Interestingly, sometimes, after a procedure called TURP (transurethral resection of the prostate, commonly performed to treat benign prostate enlargement), the PSA value can decline in the blood. Also, after a prostate examination by your doctor, there can be a very mild increase in PSA in the blood. PSA also increases after ejaculation, so you should wait for two days after ejaculation to be tested.

Some medicines and herbal remedies can lower PSA levels, and men with early stage prostate cancer who are taking them will mistakenly and tragically have normal tests results when their PSA is tested. When you are getting your PSA tested, your doctor should ask you about whether you have been taking any of the following (tell your doctor if he or she does not ask you): finasteride; androgen-receptor blockers such as flutamide, bicalutamide, and nilutamide; and PC-SPEC (an herbal mixture that contains saw palmetto).

How reliable are PSA tests (assays)?

It depends upon what you mean by that question. If you are asking whether the same blood sample sent to two different laboratories will give similar results, then the answer is yes, if both laboratories use the same type of testing procedure (assay). If the question is whether the PSA test done on the same person a few days or weeks apart will be the same, the answer is, "it depends." Physiological variations and other factors, such as infection, can affect the PSA levels. Never base a diagnosis or treatment decision on just one PSA test! There can be variability in day-to-day PSA levels.

What if my PSA does not return to zero after radical prostatectomy?

If your PSA does not return to zero after radical prostatectomy, it suggests either that the surgeon left some cancer behind in the prostate bed (see Chapter 9, "Persistent Disease After Surgery"), or that prostate cells migrated from your prostate to somewhere else in your body before the surgery, and the cancer has come back. Rising PSA can also be a sign after radiation treatment that cancer has come back: if a patient has three consecutive rises in PSA after PSA reaches its nadir [its lowest point], the cancer has returned (more on this in the section on radiation treatments). Measuring PSA is the best way available to date to make sure that your treatment for prostate cancer has cured you. However, PSA must be combined with Gleason score to estimate the growth of cancer.

Are there "other" PSA tests?

Yes, there are variations on refinements of PSA measurements. These other PSA tests can be used if your total PSA level is borderline (between 4 and 10 ng/mL). Not all physicians agree on the usefulness of these tests, however, and your doctor can help you decide which tests, if any, are right for you.

- **Percent free PSA** – This blood test tells your doctor how much PSA circulates unbound in the blood and how much is bound together with other blood

◆ Advanced Notes

What is half-life? What is PSA's half-life?

Half-life of PSA is sometimes designated as "t1/2". PSA's half-life is about 3.5 days. If a man's prostate was removed, and his PSA was 8, in 3.5 days his PSA will be 4; in 7 days, PSA will be 2; in 10.5 days it will be 1.0. PSA does not disappear from the body instantaneously; it has to be metabolized, which is a slow process. The t1/2 concept has important implications. After surgical prostate removal in some patients with prostate cancer, the PSA value should be 0 or close to 0 in about a month (if the cancer was confined to the prostate). Why? Suppose a patient's PSA was 100 before the operation. After surgery, the value should go down by 1/2 every 3.5 days. (See table 4 below.)

Table 4

Day 0	Day of Surgery	PSA = 100
Day 3.5		PSA = 50
Day 7	1 week	PSA = 25
Day 10.5		PSA = 12.5
Day 14	2 weeks	PSA = 6.25
Day 17.5		PSA = 3.125
Day 21	3 weeks	PSA = 1.56
Day 24.5		PSA = 0.78
Day 28	4 weeks	PSA = 0.39
Day 31.5	About 1 Month	PSA = 0.2

By 10 half-lives (35 days), PSA should be 0, because most PSA tests cannot detect blood levels below 0.2 (although more recent ultrasensitive tests can). Remember that, in a majority of patients diagnosed with prostate cancer, PSA values diagnosed are below 20, in which case they should reach 0 sooner.

proteins. This test is appropriate for men with PSA levels between 4 and 10, a range in which it is not clear what action needs to be taken. A low percent free PSA (usually 25% or less) suggests that prostate cancer may be present and so a biopsy may be needed to determine that. If your percent free PSA is normal, you may not need to have a biopsy.

- **PSA velocity** – tells the rate of change in the PSA value over a period of 18-24 months, using three repeated measurements. A PSA velocity over 0.75 ng/ml per year suggests that its possible that cancer is present – even though the total PSA level may be normal – and indicates that a biopsy is needed.

- **PSA density** – after you have had a TRUS, your doctor can figure out your PSA density by dividing the PSA by the size of your prostate (which was determined by the TRUS). A high PSA density suggests a greater chance of having prostate cancer. A PSA density test can help distinguish between prostate cancer and BPH, which many older men have.

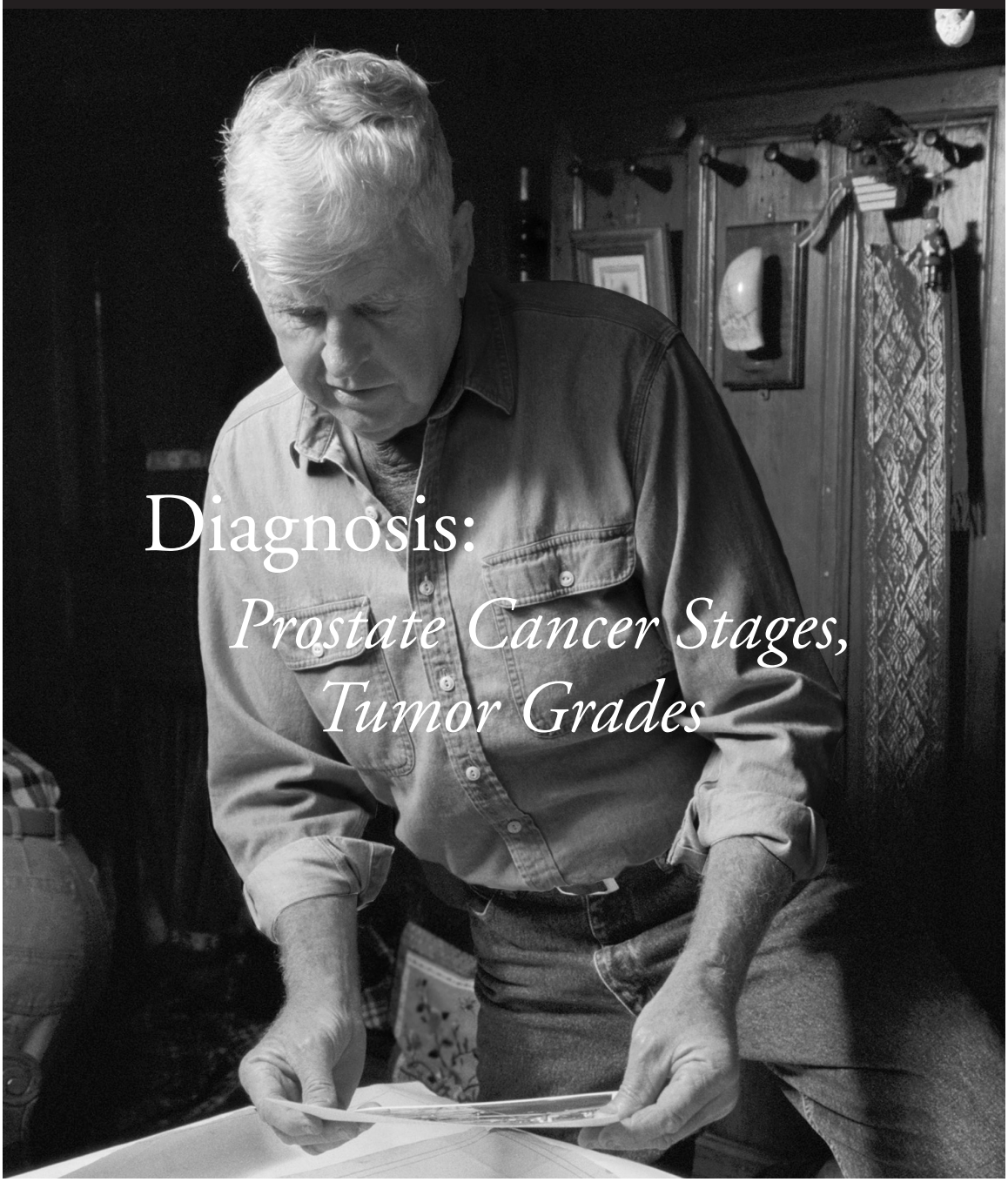
PSA testing and DRE are usually performed at the same time. Tell me about DRE.

According to the American Cancer Society, men over age 50 should have a digital rectal examination (DRE) as part of their annual health examination, to check for prostate cancer. (Men in higher risk groups, such as men with a family history of prostate cancer, or African Americans, should begin annual DREs earlier, at age 40.) In a digital rectal exam, or DRE, a doctor inserts a gloved, lubricated finger into the rectum to feel the prostate, which should be soft, smooth, and even, like the palm of your hand. (Please refer to Figure 1 at the beginning of Chapter 1 to see the male anatomy.) The prostate is located next to the rectum, and the rear of the prostate, where most prostate cancers begin, can be examined by DRE. The doctor feels the prostate for lumps, hard spots, enlargement, or irregular areas -- which might feel like the hard knuckle of your finger in contrast to the palm of your hand -- and which could be a sign of cancer. The DRE is also performed after cancer has been diagnosed to check for the spread of cancer beyond the prostate.

If your doctor feels a hard spot, he or she will want to perform additional tests, such as a biopsy, to see if it is cancer. Many other prostate conditions, such as infections, can produce the same symptoms, so it is not necessarily cancer. If your PSA has gone up, your doctor may suspect that this has happened because of an

infection, and prescribe antibiotics until the infection goes away. Then she or he will test your PSA level again, to see if it is still high. A DRE and a PSA test are generally done at the same time to detect prostate cancer, because neither test by itself is as effective as both together in detecting early cancers. Many cancers are too small to be felt by a DRE, and a DRE can miss cancers located away from the back of the prostate. Also, the usefulness of a DRE depends on the experience of the doctor performing it. However, your doctor can feel possible cancers with a DRE even when your PSA is normal, so it is an important test.

Chapter 3



Diagnosis:
Prostate Cancer Stages, Tumor Grades

Diagnostic Tests

Once prostate cancer is diagnosed, why do I go through a "staging work-up?"

You have already had two diagnostic tests, the DRE (digital rectal exam) and PSA assay, which led to your diagnosis of prostate cancer. A staging work-up is a series of tests that help the physician determine how far advanced a cancer is. Knowing whether the cancer is early-stage or advanced will help guide the physician's recommendation for method of treatment.

If your DRE is normal or reveals only a small nodule, your PSA level is less than 10, and your Gleason score from the prostate biopsy is low, this indicates that cancer is unlikely to have spread, and none of the following tests may be needed. If your physician believes there is a probability that the cancer has spread to the pelvic lymph nodes, then he or she will most likely order a bone scan and perhaps some of the following tests.

Which tests are performed to identify or rule out the spread of prostate cancer?

Note: Your physician may perform all or some of these tests.

Blood tests:

- PSA assay.
- PAP test (prostatic acid phosphatase): to determine the health of the prostate gland; an unhealthy prostate releases PAP into the blood. (This test is almost never done today.)
- Liver function tests: To rule out the spread of cancer to the liver and to check how healthy your liver is.
- BUN (Blood Urea Nitrogen) and creatinine analysis: To assess kidney function.
- CBC (complete blood count): To make sure that you are not anemic; to rule out spread of cancer to the bone marrow; and to rule out infection.

Biopsy: Perhaps you are reading this book because you learned you have a high PSA count, but have not yet had a biopsy. Even if you have had a biopsy, keep in mind that patients with suspicious first biopsy results, or with PSA levels between 4 and 10 ng/ml and a negative initial biopsy, will need a second biopsy to confirm that they do

not have cancer. Most of the men with PSA levels between 4 and 10 will have negative biopsies. Additional biopsies may be necessary as well, either of the prostate or of other parts of the body, if your doctor is checking for more advanced cancer.

A urologist usually does a prostate biopsy because the DRE or PSA test indicates that cancer might be present. A biopsy is the only certain way to detect that you have prostate cancer. The biopsy is a minor surgical procedure that takes about half an hour. In a biopsy, six to 18 tiny samples from the prostate gland are removed with a thin needle and then examined under a microscope to determine whether cancer cells are present. Samples will be taken from each part of the prostate to tell how extensive the cancer is (if there is cancer), but most of the samples will be taken from the outer area of the prostate (the peripheral zone, see the beginning of chapter one), where most cancers start growing. The doctor uses transrectal ultrasound (TRUS) to guide the needle to the prostate. The procedure lasts about an hour and you can usually go home the same day. If you have cancer, the biopsy procedure will not spread it. It is important that you do not take aspirin before the biopsy, as it would promote bleeding (ask your doctor about this, and about other medications to avoid).

There may be slight variations, but most doctors will use the procedure described above, with a thin needle and TRUS. Other rare types of biopsies are:

- inserting a needle through the perineum, the region between the scrotum and anus, rather than through the rectum
- "fine-needle aspiration cytology", another transrectal technique that sucks cells from the prostate, rather than scraping them
- "core needle" transrectal biopsies, that use large needles that obtain larger tissue samples, and require anesthesia locally or generally.

If cancer is found after a biopsy, a pathologist grades the cancer and assigns it a number based on a Gleason score (see next section). A biopsy can also identify prostatic intraepithelial neoplasia (PIN), which is often a precursor of cancer. If PIN cells are found in one biopsy, there is a chance you will have cancer detected in the next biopsy, 3-6 months later. PIN may be detected 10 or more years before cancer, however. PIN cells are abnormal and pre-cancerous, and they have their own grading system based on distinct patterns, with the mildest grade of PIN being insignificant. If PIN is detected, your doctor will want to watch you closely for any signs that cancer is developing. However, PIN by itself does not signal a need for aggressive treatment.

Side effects of a biopsy include (this is a comprehensive list, and most likely not all of these will happen to you):

- mild to severe pain or discomfort during the procedure.
- infection – should you have a fever after your biopsy, call your urologist immediately.
- blood in your bowel movements
- blood in your urine
- blood in your semen
- temporary impotence

Because it is so important to have a biopsy, do not allow fears about these possible and temporary side effects to deter your from having one.

Note: If the biopsy does not find cancer (is negative), unfortunately this does not necessarily mean that you do not have cancer. Small cancers can be missed in a biopsy (this is called a "false negative"). A repeat biopsy may be ordered if there are other signs that you may have cancer (lump felt on DRE, PSA level above 4—especially if high grade PIN is detected).

Bone scan: to detect spread of cancer into the bones. [Figures 3 and 4.] For a bone scan, a safe radioactive material (technetium) is injected into your veins, usually into your arm. Technetium "likes" bone, especially if there is trouble in the bone. A few hours after the injection, you will be placed under a machine called a gamma camera, which can detect the radioactivity. If the cancer has spread to bones, the bone scan can find it. The bones that prostate cancer usually spreads to first are the hips, pelvis, thigh bones and lower spine. Spread of prostate cancer is extremely rare in men whose PSA value is less than about 15 ng/ml. If you are having bone pain your doctor may order a bone scan. If your PSA value is low, your doctor may skip the bone scan. Bone scans are also ordered after radiation treatment if PSA levels start to rise.

Note: A bone scan is not specific for detecting cancer. Any trouble in the bone, such as a fracture, arthritis or infection, can cause a bone scan to be "positive."

Chest x-ray: To determine whether prostate cancer has spread to the lungs, or other structures, such as the ribs. However, spread of prostate cancer to the lungs is rare and is associated with advanced cancer. A chest X-ray is also helpful for a man over age 50, who smokes or has hypertension (high blood pressure). In this case, a chest X-ray may show primary lung cancer (cancer that originated in the lungs, not spread from the prostate); swelling of the heart; or infections such as tuberculosis.

Figure 3 **Figure 4**

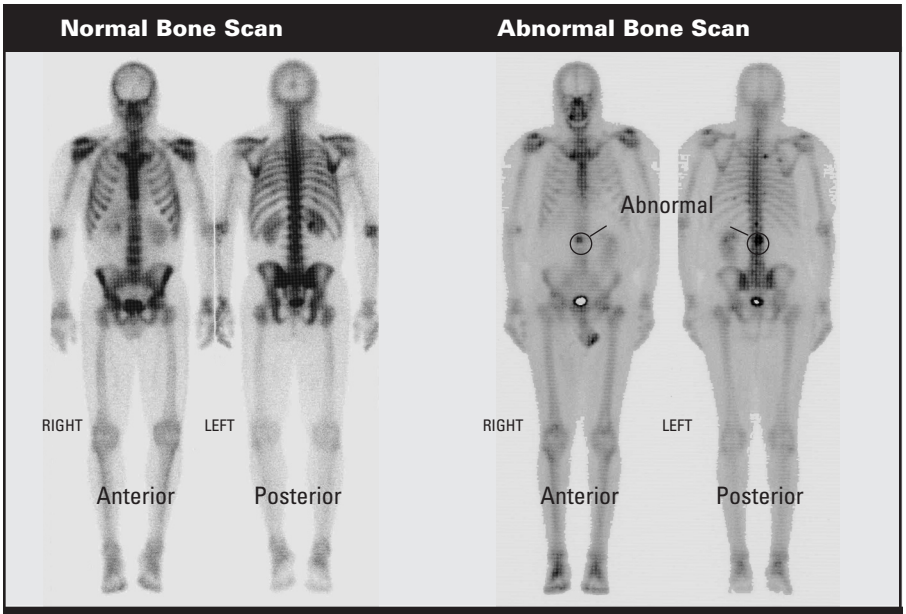
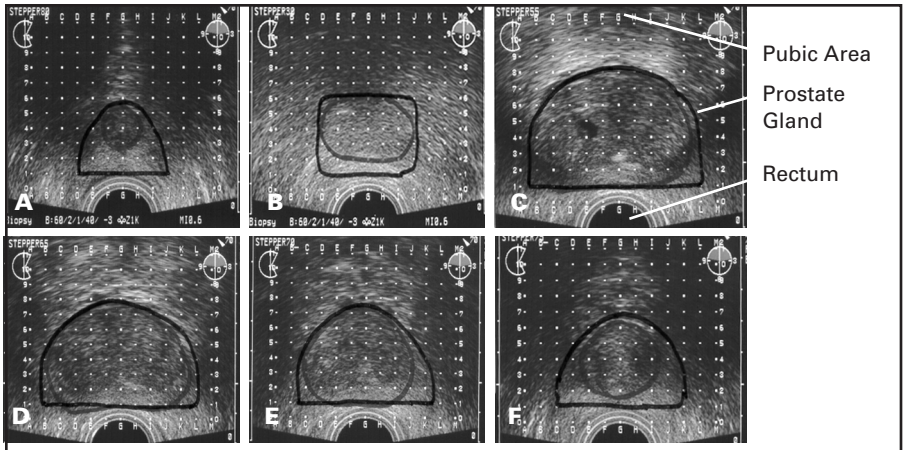


Photo of positive/negative bone scan

Doctors often use the terms "positive" and "negative" when discussing diagnoses. In physician lingo, "positive" is usually bad as it means something has been found on a diagnostic test; "negative" is usually good because nothing has been found. The circles indicate "positive" spots in the low back bone—potential cancer spread. The treatment for cancer that has spread to the bone most likely will be hormonal therapy.

Ultrasound of the prostate (transrectal ultrasound, or TRUS) (optional): You probably had an ultrasound examination when you had a biopsy during the initial diagnosis phase. A second ultrasound is not necessary unless the first one was not satisfactory. In a TRUS procedure, a small probe is placed into the rectum, which sends out sound waves at the prostate and creates a picture on a video screen. Cancer is "different" or "thicker" than normal tissue, and the sound waves bounce off of them differently. This test can detect cancer and show if the cancer has spread to nearby tissues. It is also used to estimate the size of your prostate, which then becomes part of the equation to determine PSA density. If possible cancer is detected, a biopsy will be needed to confirm that it is cancer. Tumors that are not found by DRE can be found by TRUS. An ultrasound can also ascertain if a high PSA level is due to BPH or prostate cancer. [Figure 5]

Figure 5. TRUS

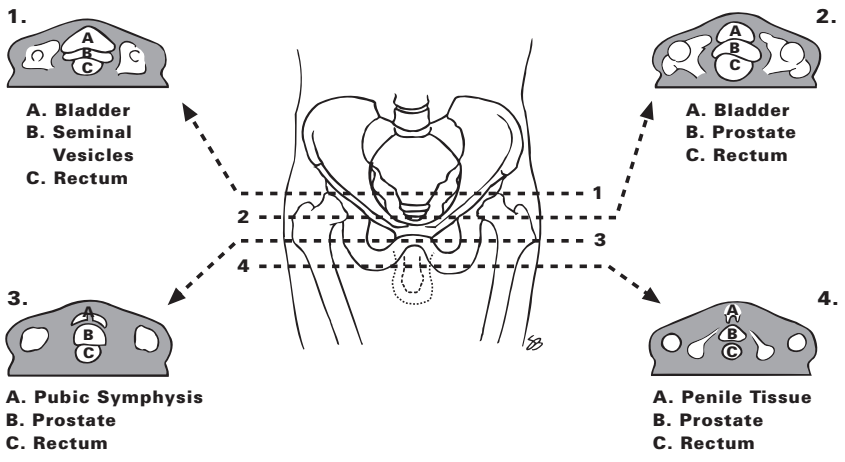


Images A-F show ultrasound images of the prostate. These images were obtained by placing a probe in the rectum. The top of each image corresponds to the pubic area; the bottom dark area to the rectum. The inked circled areas correspond to the approximate area of the prostate gland. These images are photographed starting from the top of the prostate and moving toward the bottom of the gland. Each photograph or horizontal slice of the gland is approximately 1cm apart.

CAT scan (also called "CT scan" or "CT") (optional): A CT is not necessary for a prostate cancer staging work-up unless there is a chance that cancer has spread to the lymph nodes, liver, bladder, or kidneys. Cancer spreads first to the lymph nodes when it leaves the prostate. In that case, the CAT scan will show enlarged pelvic lymph nodes, which could indicate cancer (lymph nodes can be enlarged for many other reasons too). It is an expensive test and so it won't be ordered unless your doctor thinks it is necessary, and its results will be considered along with other tests.

However, CT has other uses in the treatment of prostate cancer (in conformal radiation therapy, for example), so your physician may choose to order this test. (See conformal radiation therapy, Chapter 6.) "CT" stands for computerized tomography and "CAT" for computer-assisted tomography; both terms refer to the same procedure. CT/CAT scans are actually three-dimensional X-ray tests that provide images of cross-sectional "slices" of the body. [Figure 6]

Figure 6. CAT Scan



The center figure shows the bones of the pelvic area. 1-4 are CT ("slices") at different levels. A, B and C in each slice are labeled. The pelvic and hip bones are located on either side of A, B and C.

◆ Advanced Notes

Transrectal Coil MRI: This new test is used by some doctors for staging and assessing the volume of prostate cancer. It can show seminal vesicle or bladder involvement, and enlarged nodes or bony metastasis, with images that can be more detailed than body coil MRI or transrectal ultrasound. In expert hands, this can be an extremely useful test.

MR Spectroscopy: Also a new test, magnetic resonance spectroscopy (MRS) can enhance prostate cancer imaging. MRS detects MR signals of the cellular metabolites citrate, creatine, and choline—all potential prostate cancer markers. Normally, healthy prostate epithelial cells secrete high levels of citrate, whereas prostate cancer is associated with low citrate levels. Prostate cancer is associated with significantly decreased levels of phosphocreatine and increased levels of phosphomonoesters. MR spectroscopic imaging could improve our ability to diagnose prostate cancer. However, this imaging technique is still being tested and prostate MR spectroscopy is available only in a few centers in the country. This is likely to contribute significantly to prostate cancer patient care in the near future.

MRI scan (optional): A magnetic resonance imaging ("MRI" or "MR") scan is not done routinely. In some experts' hands, MRI gives valuable information, especially when a tube-like probe is inserted into the rectum in close proximity to the prostate. An MRI is a picture made by a high-powered magnet that shows the prostate and parts of the midsection. MRI provides a three-dimensional body scan that gives "more" information than CT scans. MRI is usually used to check for cancer spread to the lymph nodes and/or bone. However, it is perhaps not precise enough to stage cancer and MRI also shows lesions which are not cancerous as well as those that are cancerous. Some patients experience claustrophobia during the procedure inside the MRI chamber, which lasts up to one hour.

Other Diagnostic Tests

- **ProstaScint scan:** This scan uses a different type of radioactive material to find prostate-specific membrane antigen (PSMA) in the body, most likely in bones and lymph nodes. Detecting PSMA outside of the prostate suggests the prostate cancer has spread. The ProstaScint is most frequently used to detect for recurrence of cancer, rather than for staging cancer "up front". It's role is still under investigation.

- **Positron Emission Tomography (PET):** Another new scan called a PET scan is evolving to detect the initial spread of cancer to lymph nodes or distant sites or to detect the recurrence of cancer. Different radiotracers like flourodeoxyglucose (FDG), 11C or 18F choline and acetate, 11C methionine, 18F fluoride and fluorodihydrotestosterone are being investigated.

- **Lymph node biopsy (lymphadenectomy):** In this procedure, lymph nodes near the prostate are removed and examined by a pathologist. This test can be used to confirm that the cancer has not spread beyond the prostate. If a bone scan or CT scan has shown that the cancer has spread, a lymphadenectomy is not necessary. This is rarely done without a prostatectomy nowadays.

Staging Prostate Cancer

What is a "stage" of cancer?

Most cancers are categorized into four groups: stages T_1, T_2, T_3, and T_4 (also called stages I, II, III and IV, or A, B, C and D). These stages indicate the degree of severity of a cancer, and how much it has spread within the prostate or throughout the body. Determining the stage is useful for guiding treatment decisions. The lower the number or letter (for example, stage T_1 or stage I), the better the chances are for recovery. For example, if a prostate cancer is still confined to the prostate gland, then the stage is T_1(A) to T_2(B); with spread to the immediate surrounding tissues, it is stage T_3(C); if the cancer has spread widely, it is stage T_4(D).

When a doctor makes his or her estimate of the stage of a cancer, he or she is sometimes forced to make difficult judgments on borderline cases. Labeling a cancer stage as one type or another can make a difference in the treatment options offered. That's why it is important to see doctors who have a lot of experience in treating prostate cancer, and to ask questions during your office visits.

Why is the stage useful?

The stage of a cancer often:

- Indicates how early or advanced a cancer is.
- Guides decisions about treatment options.
- Helps determine the purpose of any treatment. For early-stage cancer, the goal of treatment is to cure by eradicating all of the cancer cells from the body. For advanced-stage cancer, cure may not be possible. In the advanced case, the goals of treatment can be to control further spread of the cancer, to prolong the patient's life, and/or to relieve symptoms and improve the patient's quality of life.
- The stage helps us to compare the overall historical results of alternative treatments – such as surgery versus radiation therapy – on similar stages of cancer in different men. This historical perspective can be helpful when patients are considering different treatment options.

How is prostate cancer staged?

Your physician may define your cancer stage using the terms T_1, T_2, T_3, T_4; or I, II, III, IV; or A, B, C, D (rarely used today).

The T stages are part of the TNM system, in which:

- T = tumor, and the "T" numbers describe the size of the primary tumor. (These are the T numbers given in the examples on the next two pages.)
- N = nodes, and classifies the amount of cancer spread to the lymph nodes draining the area of the primary tumor.
- M = metastasis, and refers to the extent of cancer spread ("metastasis") to distant organs, or to distant lymph nodes.

The three letters (T, N, M) are followed by a number (1-4) and sometimes a small letter (a-c). The numbers indicate the spread of the tumor. The letters represent the location of the tumor. For example, a $T_1N_1M_0$ cancer would mean that a patient has a T_1 tumor, N_1 lymph node involvement, and no distant metastases.

Some doctors use the 1997 AJCC (American Joint Committee on Cancer) version of TNM staging, while others prefer the 2002 version (there are other, older scales as well, such as the Whitmore-Jewett). Ask your doctor which he or she is using as there are slight differences—most significantly, the 1997 version combines some of the T_2, T_3, and N stages. If your doctor tells you that you have stage T_{2a} or T_{2b} prostate cancer, you need to know which TNM version he or she is using because those stages have different meanings in each version (see Table 5).

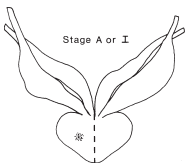
Table 5. Comparison of Different Staging Systems for Prostate Cancer

Whitmore Jewett (1956)	1997 AJCC TNM Stage	2002 and 1992 AJCC TNM Stage	Description
none	TX	TX	Primary tumor (cancer) cannot be assessed
none	T_0	T_0	No sign of primary tumor
A	T_1	T_1	Clinically unapparent cancer--tumor cannot be felt by DRE and is not visible by imaging
A_1	T_{1a}	T_{1a}	Cancer found during another procedure; cancer makes up 5% or less of prostate sample
A_2	T_{1b}	T_{1b}	Cancer found during another procedure; cancer makes up more than 5% of prostate sample
none	T_{1c}	T_{1c}	Cancer found by needle biopsy which was ordered because of a high PSA level
B	T_2	T_2	Cancer can be felt by DRE and is confined to the prostate
B_1	**T_{2a}**	**T_{2a}**	Cancer involves half of one prostate lobe or less
B_1		**T_{2b}**	Cancer involves more than half of one prostate lobe, but not both lobes
B_2	**T_{2b}**	**T_{2c}**	Cancer involves both prostate lobes
C	C	T3	Cancer extends through the prostate capsule
C_1	T_{3a}	T_{3a}	Cancer extends beyond the prostate capsule
C_1	T_{3b}	T_{3b}	Cancer invades seminal vesicles
C_2	T_4	T_4	Cancer has spread beyond seminal vesicles
none	NX	NX	Regional lymph nodes were not assessed
none	N_0	N_0	Cancer has not spread to any lymph nodes
D_1	N1	N1	Cancer has spread to one lymph node (metastasized), of a size less than 2 cm in diameter
none	MX	MX	Distant metastasis cannot be assessed
none	M_0	M_0	No distant metastasis
D_2	M_1	M_1	Distant metastasis
D_2	M_{1a}	M_{1a}	Cancer has spread to non-regional lymph nodes
D_2	M_{1b}	M_{1b}	Cancer has spread to bone(s)
D_2	M_{1c}	M_{1c}	Cancer has spread to other distant sites

Following are brief definitions of these cancer stages. [Figures 7-10]

Figure 7

Stage T_1 (also called I or A)



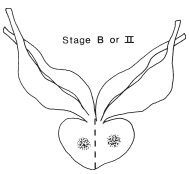
- Very early stage cancer ("latent" cancer).
- Men can have T1 prostate cancer for years without feeling any symptoms.
- Cancer is too small for physician to feel manually, but may be detected by a PSA test, or from a sample of prostate tissue taken during a biopsy or a procedure to alleviate some other prostate problem.

Stage T_{1a} (A1): The cancer is very small; less than 5% of tissue removed has cancer.

Stage T_{1b} or T_{1c} (A2): The cancer tumor is moderate size; more than 5% of tissue has cancer. T_{1c} tumors are distinguised from T_{1b} and T_{1a} in that they are found because of a biopsy called for after the discovery of an elevated PSA.

Figure 8

Stage T_2 (also called II or B)



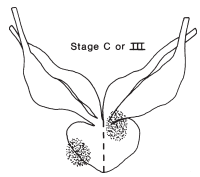
- Early stage cancer.
- The cancer can now be felt manually.
- The cancer is confined to the prostate; it has not spread to other parts of the body.

Stage T_{2a} (B1 [1997 AJCC scale]): Cancer is located on only one side of the prostate gland, and less than half, or at the most half, of that side has cancer.

Stage T_{2b} (B2 [1997 AJCC scale]): Cancer is located on both sides of the prostate gland, but has not spread outside of the prostate to surrounding tissue.

Figure 9

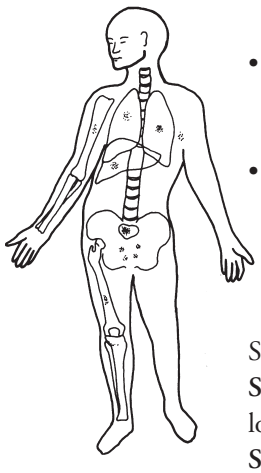
Stage T_3 (also called III or C)



- Cancer has advanced locally ("regionalized" prostate cancer).
- Cancer has spread outside the prostate gland and involves adjacent tissues such as the seminal vesicles. However, cancer has not yet spread far away in the body.
- Prostate cancer at this stage is readily detected during a DRE.
- At stage T_3, it may still be possible to completely destroy the cancer.

Figure 10

Stage T_4 (also called IV or D)



- Advanced stage of cancer. The prostate is enlarged and completely involved with cancer.
- Cancer has spread ("metastasized") through the blood to lymph nodes, bones, lungs, liver, or other distant tissues.
- At stage T_4, cancer may not be completely destroyed. Treatment focuses on preventing further spread ("metastasis"), relieving symptoms, and enhancing quality of life.

Stage D can be further subdivided.
Stage D1: Cancer cells have spread to lymph nodes located close to the prostate gland.
Stage D2: Cancer cells have spread to lymph nodes located far away from the prostate gland, and may have spread to the bones, lungs, liver or other organs or tissues.

N and M Stages

Doctors may also use some of the following names for stages:

N Stages

N_0 =	cancer has not spread to any lymph nodes (can be found in stages T_1, T_2, T_3, and T_4)
N_1 =	cancer has spread to one lymph node; it is less than 2 cm in diameter (stage T_4)
N_2 =	cancer has spread to one lymph node of between 2 cm and 5 cm in diameter; or to more than one lymph node (stage T_4)
N_3 =	cancer has spread to at least one lymph node and is larger than 5 cm in diameter (stage T_4)
N_x =	no tests have been done to detect the spread of cancer in the lymph nodes

M Stages

M_0 =	cancer has not metastasized beyond the regional nodes (found in stages T_1, T_2, T_3, and T_4)
M_1 =	distant metastases (stage 4)
M_{1a} =	distant metastases in lymph nodes (stage 4)
M_{1b} =	metastasis to bone
M_{1c} =	metastasis to other distant sites (such as lungs, liver, or brain)
M_x =	no tests have been done to detect distant spread

Should I make a decision on treatment based only on the stage?

No. Nor should you become discouraged, or allow someone else's assessment of where you stand cause you to become pessimistic. In addition to clinical staging, patients and their physicians should consider many factors before deciding on a treatment approach. Outcome estimates, based on results for other men with similar stages of prostate cancer, can provide a reasonable yet uncertain estimate of your own odds for response to a specific treatment. PSA value also should be considered, as well as tumor grade. (See Gleason Grade, next section.) In addition, factors such as age, quality of life issues, and personal preferences should be considered. (See Chapter 4 on treatment choices.)

Tumor Grades

How is the "grade" of cancer different than the "stage"?

Stage describes how much the cancer has spread beyond its original site, the prostate gland. Grade describes the degree of normalcy or abnormality of the cancer cells; in other words, how much the cancer cells do or do not look like normal, healthy cells. Higher Gleason grades also indicate several or faster-growing tumors. In prostate cancer, grade is used to describe the severity of disease, like temperature measurement in someone with a fever: 104° F is a very high fever; 100° F is a moderate fever; and 98.6° F is a normal temperature.

Describing somebody's prostate cancer by stage, grade, and PSA is like describing a person by sex, race, age, height and weight. These are basic characteristics that you will always refer back to as you learn more about your prostate cancer and consider treatment options.

Who determines the grade, and how?

Grade is determined by pathologists who study cells from the biopsy in the lab. Since the results are so critical to you, if possible you will want to have your biopsy cells reviewed by a pathologist who is an expert in prostate cancer, such as is found at a major university. First, the pathologists determine whether there is cancer. Then, if there is cancer, they determine the grade. In prostate cancer, they look for:

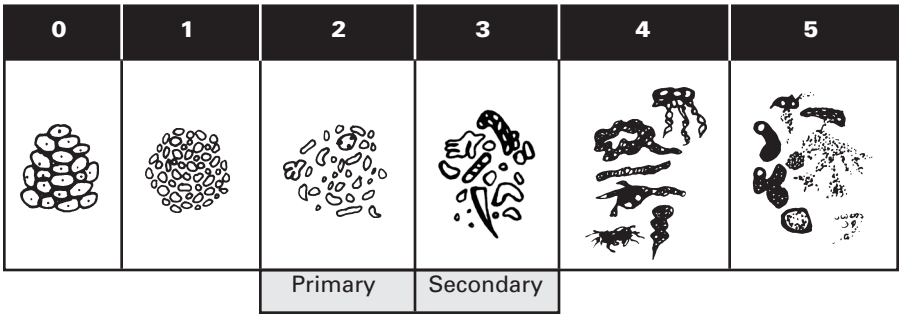
1. A primary or predominant pattern.
2. A secondary or second predominant pattern. Pattern tells how deviant the cancer cells are from normal cells; i.e., the cancer cells are being "graded."

What is the Gleason Score?

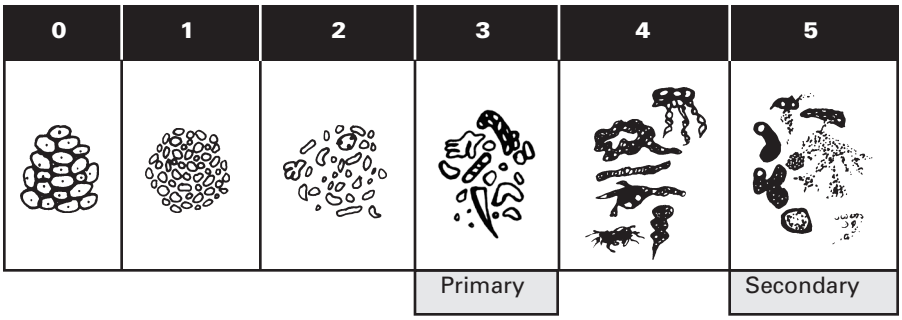
The Gleason score, or Gleason sum, is the number obtained by adding two Gleason grades together. The Gleason score will be a number from 2 to 10. The Gleason score and the Gleason grade are different. For examples, let's look at Figure 11. For patient #1, the primary cell pattern is Pattern 2; the secondary cell pattern is Pattern 3. Adding 2+3 = Gleason Score of 5. Similarly, for patient #2, the primary cell pattern is 3, the secondary cell pattern is 5, and so the total Gleason Score is 8.

Figure 11

Patient #1 with a Gleason Sum of 5.



Patient #2 with a Gleason Sum of 8.



How does the grading system work?

The most common system of cancer grading used in the U.S. is the Gleason score. The Gleason score is figured out by adding together the two most common Gleason grades. If only one Gleason grade is designated, then it is doubled to get the Gleason score. It is important to know all three numbers (the two grades that equal a score) because if you are just told one number, you could misinterpret a grade as a score. [See Figure 11] Gleason scores are as follows:

- Gleason Score 1 = cancer cells, but closely resemble normal cells
- Gleason Score 2-4 = well-differentiated cancer cells, the least severe
- Gleason Score 5-7 = cancer cells, moderately severe
- Gleason Score 8-10 = poorly differentiated cancer cells, very severe (fast growing and possibly spread beyond the prostate)

◆ Advanced Notes

Some pathologists simplify and grade tumors as 1, 2 or 3. This is also called "Broder's grading." Broder grades are defined as:

- Broder Grade 1 = well-differentiated
- Broder Grade 2 = moderately-differentiated or moderately well-differentiated
- Broder Grade 3 = poorly-differentiated

To convert Gleason Score grading to Broder's grading, one can use the following table:

- Gleason Score 2, 3 or 4 = Broder Grade 1
- Gleason Score 5, 6 or 7 = Broder Grade 2
- Gleason Score 8, 9 or 10 = Broder Grade 3

Patients with well-differentiated tumors generally respond well to cancer treatment (well-differentiated cells resemble normal prostate tissue very closely), and those with moderately differentiated tumors will do moderately well. Poorly differentiated tumors are much more difficult to treat. Though Gleason scores can range from 2 to 10, very few 2, 3 or 4 scores are diagnosed, and Gleason scores of 8, 9 or 10 are found only about 10% of the time. Most Gleason scores will be 5, 6 or 7, where there is the least agreement about the proper treatment. Be aware too that not all Gleason scores are alike: a score of 7 can be either 3 + 4, or 4 + 3. The first number is the primary grade of cells, and carries more weight. Thus, patients with a Gleason 7 score arrived at by 3 + 4 likely will do better than those with a score of 7 achieved by 4 + 3.

What do stage, grade and PSA tell about spread of cancer?

Collectively, these measurements can help predict the course of the disease and the potential that cancer has spread beyond the prostate gland. The combined data is more accurate than looking at stage, grade or PSA individually. (See Partin tables starting on the next page.)

◆ Advanced Notes

How does clinical staging differ from pathologic staging? Clinical stage is based on clinical examination and tests, whereas pathological staging is based on surgical and subsequent pathological findings. Clinical stage is used to make treatment decisions. The urologist or cancer specialist, based on results from staging work-up tests, determines clinical staging. Because it is based on test results only, clinical staging can underestimate the spread of the disease. In 20-50% of patients, a cancer classified as stage I or II by clinical staging may actually be stage III when assessed pathologically. Pathologic staging is performed when the prostate is removed during surgery and one can actually see where the cancer is, and whether it has spread to other tissues. Men who do not have surgery do not have a pathologic stage.

Partin Coefficient Tables: Prediction of Lymph Node Involvement

Introduction

The Partin Tables help you and your doctor make decisions about treatment by predicting the pathological stage before treatment; this also suggests the probability of cure. Correlating PSA, clinical stage, and Gleason score more accurately predicts the final pathologic stage better than any one of those measures by itself. Please remember that these are all useful statistics, but they are not the final word on your cancer situation. Do not become discouraged if your Partin table prognosis seems unfavorable. Whatever stage of cancer you are in, there are men whose cancer has been controlled at that stage, and others who have learned to live with cancer while leading fulfilling lives. Never lose hope. (I recommend that you read Stephen Jay Gould's essay "The Median Isn't the Message" to better understand how misleading statistics can be.)

The following four tables give data, which allow you or your doctor to predict the probability that prostate cancer has spread out of your prostate into the lymph nodes on the basis of your Gleason score, your PSA value, and your clinical stage. Be sure to use the table that is based on your PSA value.

Example

Mike is a 62-year-old man with a PSA of 8.4 ng/ml and a Gleason score of 4 + 2 = 6. His doctor has categorized his clinical stage as T_{2b} since he was able to feel a significant induration in one lobe of Mike's prostate during a digital rectal exam (DRE), and the biopsy and ultrasound indicated that the cancer had invaded more than half of that lobe. However, there was no sign of cancer in the other lobe.

Using the table for Clinical Stage T_{2b}, we find that Mike has a 2% likelihood of prostate cancer that has invaded his lymph nodes. In other words, there are about 49 chances in 50 that Mike's cancer has not invaded the lymph nodes.

Prediction of Probability of Lymph Node Involvement *Clinical Stage T_{1c}*					
PSA	Pathologic Stage (Gleason score)				
Range	2-4	5-6	3+4=7	4+3=7	8-10
0-2.5	--	--	1	1	1
2.6-4.0	--	--	1	1	1
4.1-6.0	--	0	2	3	3
6.1-10.0	--	0	2	2	3
>10.0	--	2	8	10	11

Prediction of Probability of Lymph Node Involvement *Clinical Stage T_{2a}*					
PSA	Pathologic Stage (Gleason score)				
Range	2-4	5-6	3+4=7	4+3=7	8-10
0-2.5	--	0	2	3	3
2.6-4.0	--	0	2	2	3
4.1-6.0	--	1	4	6	6
6.1-10.0	--	1	3	5	5
>10.0	--	4	14	18	17

Prediction of Probability of Lymph Node Involvement *Clinical Stage T_{2b}*					
PSA	Pathologic Stage (Gleason score)				
Range	2-4	5-6	3+4=7	4+3=7	8-10
0-2.5	--	1	4	6	6
2.6-4.0	--	1	3	4	5
4.1-6.0	--	2	7	10	10
6.1-10.0	--	2	6	8	8
>10.0	--	8	22	27	27

Prediction of Probability of Lymph Node Involvement *Clinical Stage T_{2c}*					
PSA	Pathologic Stage (Gleason score)				
Range	2-4	5-6	3+4=7	4+3=7	8-10
0-2.5	--	1	6	9	10
2.6-4.0	--	1	5	7	8
4.1-6.0	--	3	12	16	16
6.1-10.0	--	3	10	13	13
>10.0	--	13	33	38	38

All numbers represent percent predictive probabilities (95% confidence interval); ellipses indicate lack of sufficient data to calculate probability. Reprinted with permission from Alan Partin, MD.

Partin Coefficient Tables: Prediction of Probability of Organ-Confined Disease

Introduction

The following four tables give data that allow you or your doctor to predict the probability that you have organ-confined prostate cancer on the basis of your clinical stage, PSA, and Gleason score. Be sure to use the table that is based on your clinical stage.

Note that the data given in these four tables are roughly the reverse of the data in the tables predicting the probability of a patient having established capsular penetration.

Example

Cecil is a 59-year-old man with a PSA of 59.3 ng/ml and a Gleason score of 4 + 5 = 9. His doctor has categorized his clinical stage as T2C since he could clearly feel what appeared to be abnormalities in both lobes of Cecil's prostate on DRE.

Using the table for clinical stage T_{2c}, we find that Cecil has only a 6% likelihood of organ-confined disease (equivalent to a 94% probability of established capsular penetration). In other words, it is all but certain that the cancer has penetrated into Cecil's prostate capsule.

* *Partin tables are reproduced with permission from Alan Partin, MD, and the journal Urology. Source: Partin AW, Mangold LA, Lamm DM, Walsh PC, Epstein JI, Pearson JD. Contemporary update of prostate cancer staging nomograms (Partin Tables) for the new millennium. Urology. 2001 Dec;58(6):843-8.*

Prediction of Probability of Organ-Confined Disease *Clinical Stage T_{1c}*					
PSA Range	Pathologic Stage (Gleason score)				
	2-4	5-6	3+4=7	4+3=7	8-10
0-2.5	95	90	79	71	66
2.6-4.0	92	84	68	58	52
4.1-6.0	90	80	63	52	46
6.1-10.0	87	75	54	43	37
>10.0	80	62	37	27	22

Prediction of Probability of Organ-Confined Disease *Clinical Stage T_{2a}*					
PSA Range	Pathologic Stage (Gleason score)				
	2-4	5-6	3+4=7	4+3=7	8-10
0-2.5	91	81	64	53	47
2.6-4.0	85	71	50	39	33
4.1-6.0	81	66	44	33	28
6.1-10.0	76	58	35	25	21
>10.0	65	42	20	14	11

Prediction of Probability of Organ-Confined Disease *Clinical Stage T_{2b}*					
PSA Range	Pathologic Stage (Gleason score)				
	2-4	5-6	3+4=7	4+3=7	8-10
0-2.5	88	75	54	43	37
2.6-4.0	80	63	41	30	25
4.1-6.0	75	57	35	25	21
6.1-10.0	69	49	26	19	15
>10.0	57	33	14	9	7

Prediction of Probability of Organ-Confined Disease *Clinical Stage T_{2c}*					
PSA Range	Pathologic Stage (Gleason score)				
	2-4	5-6	3+4=7	4+3=7	8-10
0-2.5	86	73	51	39	34
2.6-4.0	78	61	38	27	23
4.1-6.0	73	55	31	21	18
6.1-10.0	67	46	24	16	13
>10.0	54	30	11	7	6

All numbers represent percent predictive probabilities (95% confidence interval); ellipses indicate lack of sufficient data to calculate probability. Reprinted with permission from Alan Partin, MD.

Partin Coefficient Tables: Prediction of Seminal Vesicle Involvement

Introduction

The following four tables give data which allow you or your doctor to predict the probability that prostate cancer has spread out of your prostate into the seminal vesicles on the basis of your clinical stage, Gleason score, and PSA. Be sure to use the table which is based on your clinical stage.

Example

Gary is a 70-year-old man with a PSA of 3.2 ng/ml and a Gleason score of 2 + 3 = 5. His doctor has categorized his clinical stage as T_{1c} since he found a very small amount of cancer in tissue removed during a transurethral resection of the prostate (a TURP), which had been carried out to relieve Gary's problem with frequent and incomplete urination.

Using the table for clinical stage T_{1c}, we find that Gary has a 1% likelihood of prostate cancer involving his seminal vesicles. In other words, it is all but certain that Gary's cancer does not extend into the seminal vesicles.

** Author's Note: These tables from one institution may not exactly match data from other institutions. These tables should be used as approximate estimates.*

Prediction of Probability of Seminal Vesicle Involvement *Clinical Stage T_{1c}*					
PSA Range	Pathologic Stage (Gleason score)				
	2-4	5-6	3+4=7	4+3=7	8-10
0-2.5	--	0	2	2	4
2.6-4.0	--	1	4	4	6
4.1-6.0	--	1	3	3	5
6.1-10.0	--	2	8	8	13
>10.0	--	4	12	11	17

Prediction of Probability of Seminal Vesicle Involvement *Clinical Stage T_{2a}*					
PSA Range	Pathologic Stage (Gleason score)				
	2-4	5-6	3+4=7	4+3=7	8-10
0-2.5	--	1	5	4	7
2.6-4.0	--	2	7	6	10
4.1-6.0	--	1	5	5	8
6.1-10.0	--	4	13	11	17
>10.0	--	6	16	13	19

Prediction of Probability of Seminal Vesicle Involvement *Clinical Stage T_{2b}*					
PSA Range	Pathologic Stage (Gleason score)				
	2-4	5-6	3+4=7	4+3=7	8-10
0-2.5	--	2	6	5	9
2.6-4.0	--	2	9	7	12
4.1-6.0	--	2	7	5	9
6.1-10.0	--	5	16	13	19
>10.0	--	8	17	13	19

Prediction of Probability of Seminal Vesicle Involvement *Clinical Stage T_{2c}*					
PSA Range	Pathologic Stage (Gleason score)				
	2-4	5-6	3+4=7	4+3=7	8-10
0-2.5	--	1	5	5	8
2.6-4.0	--	2	8	6	10
4.1-6.0	--	2	6	4	7
6.1-10.0	--	5	13	11	16
>10.0	--	6	13	10	15

All numbers represent percent predictive probabilities (95% confidence interval); ellipses indicate lack of sufficient data to calculate probability. Reprinted with permission from Alan Partin, MD.

Partin Coefficient Tables: Prediction of Extraprostatic Extension

Introduction

The following four tables give data which allow you or your doctor to predict the probability that prostate cancer has spread outside of the capsule, or covering, of your prostate to tissues around the prostate (stage T_3). As with the other tables, these are based on your Gleason score, PSA value, and clinical stage. Be sure to use the table that is based on your PSA value.

Example

Richard is a 65-year-old man with a PSA of 11.5 ng/ml and a Gleason score of 3 + 3 = 6. His doctor has categorized his clinical stage as T_{1c} since a tumor was identified by needle biopsy due to elevated PSA.

Using the table for clinical stage T_{1c}, we find that Richard has a 33% likelihood of prostate cancer with extraprostatic extension. In other words, he has a one in three chance that the cancer has extended beyond the covering of his prostate.

Prediction of Probability of Extraprostatic Extension *Clinical Stage T_{1c}*					
PSA Range	Pathologic Stage (Gleason score)				
	2-4	5-6	3+4=7	4+3=7	8-10
0-2.5	5	9	17	25	28
2.6-4.0	8	15	27	37	40
4.1-6.0	10	19	32	42	45
6.1-10.0	13	23	36	47	48
>10.0	20	33	43	51	50

Prediction of Probability of Extraprostatic Extension *Clinical Stage T_{2a}*					
PSA Range	Pathologic Stage (Gleason score)				
	2-4	5-6	3+4=7	4+3=7	8-10
0-2.5	9	17	29	40	42
2.6-4.0	15	27	41	52	53
4.1-6.0	19	32	46	56	58
6.1-10.0	24	37	49	58	57
>10.0	35	47	49	55	52

Prediction of Probability of Extraprostatic Extension *Clinical Stage T_{2b}*					
PSA Range	Pathologic Stage (Gleason score)				
	2-4	5-6	3+4=7	4+3=7	8-10
0-2.5	12	22	35	45	46
2.6-4.0	20	34	47	57	57
4.1-6.0	25	39	51	60	59
6.1-10.0	31	44	52	60	57
>10.0	43	52	47	50	46

Prediction of Probability of Extraprostatic Extension *Clinical Stage T_{2c}*					
PSA Range	Pathologic Stage (Gleason score)				
	2-4	5-6	3+4=7	4+3=7	8-10
0-2.5	14	24	36	45	47
2.6-4.0	22	36	48	57	57
4.1-6.0	27	40	50	57	57
6.1-10.0	33	46	52	58	56
>10.0	46	51	42	43	41

All numbers represent percent predictive probabilities (95% confidence interval); ellipses indicate lack of sufficient data to calculate probability. Reprinted with permission from Alan Partin, MD.

Chapter 4

Take Time to Make the Best Choice for Yourself

Most prostate cancers develop in older men and grow rather slowly, so they should not be handled as an emergency that requires an immediate decision about treatment. Be sure to take enough time to learn about your different options for treatment, ask a lot of questions, and consider all of the issues. It's important not to rush into a decision about treatment, and not to lose hope. Don't sign any papers or agree to any treatment regimen until you have read all the information you want, discussed it with family members or confidants, and have thought about it for at least a week (except when prostate cancer should be handled as an emergency -- see below). In addition to this guidebook and other information provided by your physician, you might want to find out more about prostate cancer and treatment options. Information is available at your local library, on the Internet, and from other sources. (See Reference Sources at the end of this book.)

I also recommend talking to other prostate cancer patients about their experiences, which you can do by contacting organizations such as the American Cancer Society (which has a "Man to Man" support group program; on the internet go to www.cancer.org or call 1-800-ACS-2345). The cancer center nearest to you will also know of support groups. Do this before you choose your treatment. You cannot have too much information, and cancer is too serious a concern to keep to yourself. Patients who learn as much as possible about their disease make better treatment decisions and have the best outcomes. Once you begin treatment, you should also continue to follow the details regarding your treatment, such as knowing the dimensions and location of your tumor, and get copies of all your medical records (such as pathology reports)--your goal should be to become an expert on prostate cancer.

Take Time to Think It Over

If you have just learned you have prostate cancer, you're undoubtedly overwhelmed with fears, concerns and questions. Try to relax. Take a deep breath and exhale slowly. Things will look better in the morning. These steps may help you feel less overwhelmed.

1. Drive home carefully, or have someone else drive you home.
2. Eat a nice dinner and, perhaps, enjoy a glass of fine wine.
3. Sleep well, or at least try to get a good rest.
4. Take a few days off from work.
5. Learn as much as you can about prostate cancer. Go to a book store or library and get some books about prostate cancer. If you have access to the Internet, look for information about prostate cancer. (See Reference Sources for good websites.)
6. Complete the questionnaire at the beginning of this chapter. Your responses provide a general indication of your prognosis.

When is prostate cancer an emergency?

In most cases, treatment of prostate cancer is not urgently needed on the same day the cancer is found. However, a few conditions do warrant immediate medical attention. Conditions requiring immediate treatment include:

- When there is a bone fracture resulting from the spread of cancer to the bone. (The person will be in severe pain.)
- When cancer is compressing the spinal cord.
- If cancer has spread to the brain (very rare with prostate cancer).
- If you are unable to urinate.
- If there are other unexplained, serious problems.

Questionnaire: Making the Best Treatment Choice for Me

Before choosing a treatment option, it's wise to evaluate your overall health condition and your personal priorities. This checklist will be helpful in guiding your decision-making process by providing some indication of your prognosis for cancer remission. It will also help you weigh the importance to you of personal issues such as sexual function.

1 **My age:** under 60 60-68 69-72 over 72

2 **Do I have (or have I had) any of the following conditions?**

Diabetes	☐ Yes	☐ No
Hypertension	☐ Yes	☐ No
Heart Attack	☐ Yes	☐ No
Stroke	☐ Yes	☐ No
Heart Surgery	☐ Yes	☐ No
Heart Failure	☐ Yes	☐ No
Previous Prostate Surgery	☐ Yes	☐ No

3 **I can climb** (circle one):
0 1 2 3
flights of stairs without getting short of breath.

4 **Medications I take**
(daily or frequently)

☐ None

1) _____

2) _____

3) _____

4) _____

5 **My sexual desire is** (circle one):
High Fair Low None

6 **My penile erections are:**
High Moderate Low None

7 **My sexual function is:**
☐ Very important to me
☐ Moderately important to me
☐ Not important to me

8 **My cancer stage** (circle one):

a T_{1a} T_{1b} T_{1c} T_{2a} T_{2b}
T_{2c} T_{3a} T_{3b} T_{3c} T_4
(This staging classification is preferred)

b A_1 A_2 B_1 B_2 C_1 C_2 D_1 D_2

c Non-metastatic Metastatic

9 **My Tumor Grade**
or Gleason Score:
2 3 4 5 6
7 8 9 10

10 **My PSA** _____
Date _____
Value _____
Type of Assay _____

What do the answers mean?

This questionnaire provides a rough indication of your chances for a cure and helps identify your personal priorities. The most important factors to consider when deciding on a treatment will be your age (and how long you are likely to live), health (comorbidities), goals for treatment, and willingness to deal with treatment side effects. You must honestly ask yourself some hard questions and decide what is most important to you. Your responses here are just one aspect of the decision-making process regarding your treatment. It's important to discuss the options and probable outcomes with your physician, family members or other important people in your life. Yours will be an individualized treatment plan, not one made with a cookie cutter approach. There is no easy answer in choosing treatment for prostate cancer. Your body is unique and we do not know exactly how yours will respond to cancer or its treatment. Besides the known variables, there is the chance variable of good or bad luck. As Anatole Broyard said, "The important thing is the patient, not the treatment."

1. Age

Men under age 60 typically have many more years to live, so "watchful waiting" is not a good treatment option for these men. If you have localized prostate cancer and expect to live many more years, you should choose a treatment that is intended to cure you of cancer. Also, since it is likely that a man under 60 still has good sexual function, it is especially important to consider how quality of life may be affected by potential complications of certain treatments.

For men over age 75, the opposite may be true. Older men may want to choose treatments that relieve symptoms and/or control the cancer for the rest of their lives, rather than try to cure the disease, if they do not believe that they will live long enough to benefit from the curative treatment. Surgery is much harder on older men than younger men, for example. Admittedly, determining how much longer you have to live is very difficult—and it can only be a guess—but it is crucial in choosing treatment options. If you do not expect to live more than 10 years, it may not be worth experiencing treatment side effects.

How can I determine how long I may live?

The U.S. Department of Health and Human Services, Centers for Disease Control (CDC) and Prevention, National Center for Health Statistics has actuarial tables on-line which you can consult to help you determine your life expectancy (http://www.cdc.gov/nchs/products/pubs/pubd/lftbls/life/1966.htm). You should

also discuss what your life expectancy might be with your doctor. Your diet, alcohol consumption, smoking, family history, height and weight, and other illnesses you have had (doctors call these comorbidities) will affect the life expectancy figure you get from the CDC tables.

2. Other health problems

If you have numerous other health problems or pre-existing conditions ("comorbidities"), you may be a poor candidate for surgical treatment because of the risk of surgical complications. However, you may be a candidate for radiation therapy. Men in poor health who are not experiencing any symptoms from prostate cancer may choose to have no treatment, and live with prostate cancer as a chronic disease.

3. Climbing stairs (i.e., physical fitness)

Ability to climb stairs gives an indication of your level of physical fitness. If you are more physically fit, recovery from treatment may be swifter.

4. Medications

Some medications may interfere with or affect treatment. Be sure your physician knows about all prescription or over-the-counter medications you take regularly.

5-7. Sexual desire, penile erections, sexual function

Answers to these questions do not indicate the potential for cancer remission. However, they will help you and your physician understand how different treatment options may affect your lifestyle.

Chances for a Cure

The stage of your cancer is a very important piece of information to know when it comes to selecting the treatment that is best for you.

	Good	**Not as good**
8. Cancer stage	A_1-B_2	C_1-D_2
	T_1-T_2	T_3-T_4
9. Gleason Score	2-6	7-10
10. PSA value	under 10	over 10

Involving Your Partner

You need to talk with your wife or partner about your prostate cancer and your different treatment options, before you decide on a treatment. Sexuality can be very difficult for men to talk about, particularly when you will be discussing issues such as the possibility of impotence. However, your wife or partner needs to be informed and be a partner in your treatment decisions (you can start by giving her this book to read). You may be surprised that you two might view issues of sexuality differently. For example, sexual contact includes touching and hugging, which are not affected by impotency. Ideally, your doctor will discuss these issues with you, but he or she may not have enough time to do so well, and may not be good at it. It is too easy, for your doctors and you, to focus on the facts at hand, such as your PSA, Gleason score, and cancer stage, and push the emotional issues to the side. This is a mistake. Your prostate cancer is not just affecting you. It is affecting your wife (or partner) and your children and extended families and friends. The natural tendency is to avoid the topic, but most likely they want to help and are waiting for cues from you as to how they can. Often, your fears can be relieved through discussion. Please do not fight your cancer alone – discuss it with others and ask them for help.

I can't understate the importance of spirituality. Your positive attitude and spiritual beliefs have a strong influence on your health, and can be tapped into to promote your healing and cope with cancer. Your spirituality can be a source of hope, meditation, and social connection, and can assist your healing process because they benefit your immune system and promote relaxation. So if spirituality is part of your life, do not neglect it while you focus on treatment options. Spirituality can be a partner to traditional medical care.

Some Words to the Patient's Wife or Partner

To wives and partners: While dealing with your husband's prostate cancer, you need to take care of yourselves too. Exercise, eat right, and get enough sleep. As a partner of a person with cancer, you are going through just as difficult a time as they are. You may be angry that this cancer is upsetting your plans and have fears of being left alone or left with a person who might be different than the one you knew before cancer struck. Perhaps you are feeling guilty, or having regrets, or blaming your husband – all of these are legitimate feelings. But you need to gather your strength so that you can help out in what will be a long recovery period. For example, you can take responsibility for making sure that your partner is getting proper nutrition during his recovery period, which will help him recover more quickly. Partners can also be educators and motivators, record keepers and advocates. Be sure to ask other family members, and your friends, for help. You should try to anticipate the problems that might come up and discuss them openly. There may be subtle changes to your relationship because of cancer, yet this period can also make your marriage stronger than ever, as you identify what really matters to you. Cancer can make your partner and you focus on what is really important in life, appreciate one another more genuinely, grow emotionally and spiritually, and lead to positive changes as you plan your lives after prostate cancer. How you face cancer together, starting before treatment begins, can have a big effect on how well recovery proceeds.

Choosing Your Physicians

Now, you need a team of doctors to handle your prostate cancer. A majority of American men are diagnosed at a relatively early stage of prostate cancer, and the diagnosis was made because:

- Your family doctor or internist ordered a PSA blood test, and the PSA level was elevated.
- The physician felt a prostate nodule during a digital rectal prostate examination (DRE).
- Urinary symptoms or sexual symptoms led you to see a urologist.

After going through the diagnostic process, you will already have met two of the three or four doctors you will need for your cancer care: your family doctor or internist, and a urologist, who probably did the biopsy. (In some cases, a radiologist performs the biopsy.)

If you have an early stage cancer (stage A or B/T_1 or T_2) or moderately advanced cancer (stage C or T_3) and there is no evidence of spread to other organs ("non-metastatic"), you need to talk to one more doctor: a radiation oncologist. Because the two major options for treatment are surgery (performed by your urologist) or radiation therapy (performed by a radiation oncologist), you need them both.

If your cancer is far advanced and you require chemotherapy, then you will also need a medical oncologist, who administers chemotherapy.

Your internist, urologist, radiation oncologist or medical oncologist can administer hormones, which are often used to treat prostate cancer.

Select a Cancer Team That Suits You

Now is a good time to determine if the doctors who made the initial diagnosis are the team you want to treat your cancer. Feel free to ask them questions about their approach to prostate cancer, their access to the latest innovative therapies, and their preference for surgical or minimally surgical treatment. Don't hesitate to get a second opinion elsewhere, or to turn to a different team of doctors for care. However, don't make the mistake of seeing several doctors in the same specialty; most doctors in the same specialty tend to be biased toward a particular form of treatment; for instance, radiation oncologists naturally prefer radiation treatments, whereas urologists want to operate. Select at least two doctors, one from each specialty, who are willing at least to tell you all options with fairness. If your urologist or radiation oncologist does not specialize in prostate cancer, you should see one who does. Choose doctors with a great deal of experience in the specific treatment you are selecting. The more skilled your doctor is, the less risk there is for you of experiencing side effects, and the greater the chance for successful treatment of your cancer. The skill of your doctor and your own personal outlook are very important factors influencing how well you will recover from this disease.

After learning all you can about prostate cancer and how to treat it, and meeting several doctors, you have to decide on which one doctor you are comfortable with as the leader of the team providing your care. Only that doctor can be objective

about what needs to be done, and you must trust him or her and accept his or her advice, without second-guessing. Take the time to find the best doctor that you can, but then trust him or her to do their best for you.

Many academic medical centers offer an integrated multidisciplinary team approach to cancer care. In this case, urologists, radiation oncologists, medical oncologists, pathologists and other specialists consult together and – as a unified team – make a recommendation for the most effective therapy to meet the patient's individual needs. Make sure that you talk to each specialist one-on-one, not together. Physicians tend not to differ with their colleagues in a group, so the dominant personality will have his/her say. When selecting a cancer team, look for doctors who are specialists in treating prostate cancer. Many organizations can help you identify prostate cancer experts in your area. *(See Reference Sources at the end of this book.)*

Physician Team

I may need the following people to coordinate my treatment and care:

a) My Family Doctor/Internist: _____

Phone: _____ Fax: _____

b) My Urologist: _____

Phone: _____ Fax: _____

c) My Radiation Oncologist: _____

Phone: _____ Fax: _____

d) My Medical Oncologist: _____

(only if my cancer is metastatic or recurrent)

Phone: _____ Fax: _____

e) My Nurse: _____

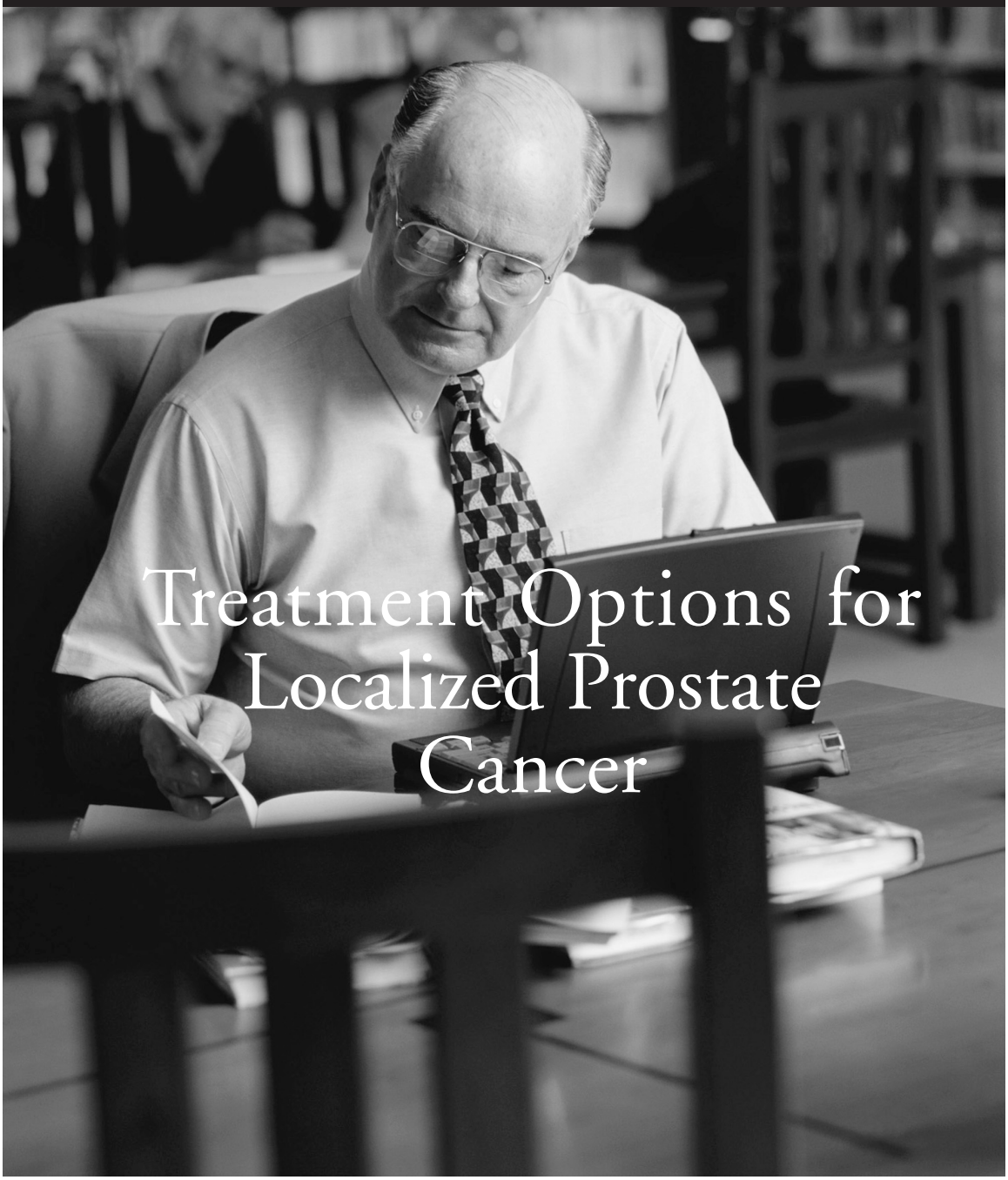
Phone: _____ Fax: _____

Evaluating the Physician Team:

a)	Do my doctors know each other?	☐ **Yes**	☐ **No**
b)	If not, have the physicians talked to each other?	☐ **Yes**	☐ **No**
c)	Are they team players?	☐ **Yes**	☐ **No**
d)	If they are not already an established team, are the physicians willing to communicate with each other about my care?	☐ **Yes**	☐ **No**
e)	Are my doctors board-certified?	☐ **Yes**	☐ **No**
f)	Are they experienced in treating prostate cancer?	☐ **Yes**	☐ **No**
g)	Do my doctors know the long-term outcomes of their patients? What are they?	☐ **Yes**	☐ **No**
h)	Can I contact a few of their patients? (Do this to learn how they are treated and how they feel about their doctor.)	☐ **Yes**	☐ **No**
i)	What are my treatment options?	☐ **Yes**	☐ **No**
j)	What will happen if I don't treat the cancer?	☐ **Yes**	☐ **No**
k)	Which treatment do you recommend, and why?	☐ **Yes**	☐ **No**
l)	How long will it take to know if the treatment has worked or not?	☐ **Yes**	☐ **No**
m)	What are the side effects, and how long do they last?	☐ **Yes**	☐ **No**
n)	If the treatment fails, what will my options be?	☐ **Yes**	☐ **No**
o)	How can I get in touch with you if I have questions?	☐ **Yes**	☐ **No**
p)	What kind of help will I need at home after treatment, or during treatment?	☐ **Yes**	☐ **No**

(For easy reference, this table also appears on the last page of this book.)

Chapter 5



Treatment Options for Localized Prostate Cancer

Which treatment is right for me?

Choosing a treatment for prostate cancer is difficult because there are many choices for localized disease and it can be hard to figure out which men will benefit from treatment and which men would be better off avoiding the treatments and their side effects. In reaching a decision, you should discuss with your doctor variables such as your age, stage of cancer, your health, and the risks and benefits of each treatment. You should not use the information in this book without discussing it with your doctor.

What is localized prostate cancer?

Cancer that has not spread to the bones, lungs, liver or lymph nodes is considered "localized." In medical language, T_1, T_2, T_3 cancers which are "N_0" and "M_0" are considered localized. (See staging figures 7-10 in Chapter 3.) When prostate cancer is localized, it is still curable, and you must decide what treatment you will choose to try to cure your prostate cancer.

Note the following:

N_0 means: "lymph nodes zero." In other words, the lymph nodes are not involved with cancer.

M_0 means: "no metastases." In other words, cancer has not spread via the blood to other body organs.

Technically, a man with T_4 N_0 M_0 cancer has a localized prostate cancer. (T stands for "tumor.") However, T_4 is so advanced locally that it needs a special approach.

What are the treatment options?

There are a variety of treatment options for localized prostate cancer. Each option should be considered carefully, balancing the advantages against the disadvantages as they relate to the individual man's age, overall health and personal preferences. Today, because of advances in treatments, patients are experiencing fewer treatment-related side effects and are living longer.

Standard options include:

- Surgery (radical prostatectomy).
- Radiation therapy (external X-ray treatments).
- Watchful waiting (no treatment, with careful observation and medical monitoring).

Newer, advanced options have been developed in the past 5-10 years. These newer options avoid or minimize some of the unpleasant side effects sometimes associated with the standard therapies.

Newer options include:
- Nerve-sparing radical prostatectomy.
- Conformal radiation therapy.
- Radioactive seed implant therapy.
- Cryotherapy.
- Proton beam therapy.

(For more on these newer, advanced options, see Chapter 6.)

Each of these standard and advanced therapy options offers pros and cons. The following chapters in this book discuss these options. Consult with your physician team for more details. Remember, too, that not all treatment options are available in all radiation therapy or urology offices. Universities with cancer centers have the most comprehensive and newest treatments.

Standard Treatment Options

Radical Prostatectomy

These two words describe the procedure well. "Radical" means something major or significant; "ectomy" in medical terms means taking out or removing. So, "radical prostatectomy" means an operation in which the entire prostate gland is removed by surgery, along with the attached seminal vesicles and some tissue around it. Radical prostatectomy is sometimes combined with hormonal therapy. In radical prostatectomy, the cancerous tumor is surgically cut out of the body and is sent to a pathologist. However, radical prostatectomy is more than that. Generally, the surgeon first samples a few lymph nodes to see whether the cancer has spread; he/she usually goes ahead with the rest of the procedure only if there is no spread. "Lymph node dissection" means removing certain lymph nodes that drain from the prostate gland.

Nodal Dissection

Modern nodal dissection (or sampling) is much safer than in the past, and now produces fewer complications. Previously, surgeons removed an extensive number of lymph nodes, resulting in swelling of the scrotum and sometimes of both legs. Today, only a few lymph nodes are removed.

To understand the scope and implications of radical prostatectomy, one needs to understand the anatomy of the prostate gland and surrounding tissues. [Figure 12a]

The prostate gland is situated in a narrow, blind cave: the pelvis. It is located in the lower third of the abdomen. In women, the pelvis is where babies grow until childbirth. The pelvis in both men and women is like a fortress with few safe openings.

This pelvic fortress is surrounded on all sides by bones (pelvic bones), which are, in turn, padded with muscles and fat. The reason nature is so protective is the content of the pelvis: the urinary bladder (where urine is stored before evacuation), the rectum (the last part of the bowel), and all kinds of blood vessels and nerves. In women, the pelvis also protects the uterus or womb. In men, the pelvis protects the prostate and seminal vesicles.

The pelvis tends to be rounder and roomier in women (for obvious reasons) than in men; the male pelvis tends to be narrow, like a triangular cave. This is problematic because, during radical prostatectomy, surgeons must work in a very narrow space, which contains many other vital structures. A radical prostatectomy (RP) is major

Figure 12a

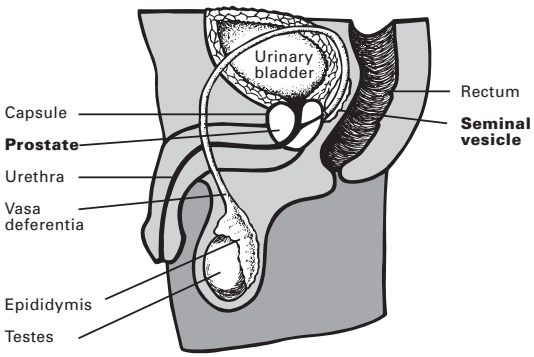


Figure 12a: Normal anatomy.

Figure 12b

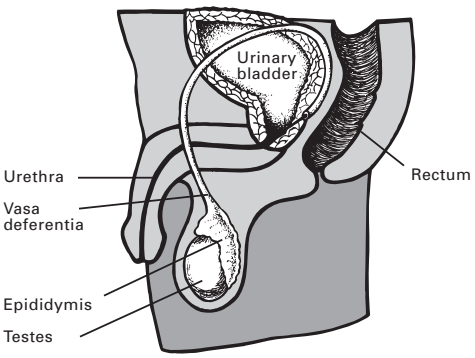


Figure 12b: Prostate and seminal vesicles have been removed. Note that the bladder has been reattached to the uretha.

surgery requiring hospitalization. However, great improvements have been made in RP compared to years ago. It no longer is the rule that men will become impotent and incontinent after this surgery, and surgical technique has improved so that there is no longer the large loss of blood that previously always occurred during a RP.

In surgeries performed for cancer, the surgeon generally aims to take out the cancer with a wide margin of healthy tissue. This helps to assure that stray cancer cells in the surrounding tissues are removed along with the tumor. For example, the margin around the cancerous tumor in patients with breast cancer is usually several centimeters (about one inch). However, because the bladder, rectum and other vital structures are located quite close to the prostate gland, it is impossible to achieve such wide margins in radical prostatectomy (RP). Generally, the margin of normal, non-cancerous tissues removed during RP is measured in millimeters (tenths of an inch). This is a major problem for RP because it may mean that, after surgery, a few stray cancer cells can be left behind in the tissue that surrounded the diseased prostate.

During surgery, the prostate gland, the urethra (the tube which carries urine through the prostate) and seminal vesicles are removed. The bottom end of the urinary bladder is lowered in the pelvis and then attached to the upper end of the penile urethra to restore the continuity of the urinary passage. [Figures 12a and 12b]

Am I a candidate for radical prostatectomy?

You might be a candidate for radical prostatectomy if:

- You have cancer that is confined to the prostate (stage T_1 or T_2)
- You are young (young people tolerate surgery better than old people)
- You are healthy (other than having prostate cancer), with very few comorbities
- Your life span is expected to be at least 10-15 years, or more than the cancer probably would let you live
- You've had no prior pelvic surgery
- You have very few comorbidities

Why are seminal vesicles removed in radical prostatectomy?

The seminal vesicles lie next to the prostate. In fact, the right and left seminal vesicles straddle the prostate gland like the two wings of a bird attached to the prostate gland, and the tubes from the seminal vesicles pierce the prostate gland. Because of the proximity, any cancer in the prostate can (and often does) spread to the seminal vesicles. Therefore, the seminal vesicles are removed because they are a likely location of cancer cells.

The function of the seminal vesicles is to store the semen and sperm until ejaculation. Note that ejaculations will be dry after Radical Prostatectomy.

Why is the urethra within the prostate removed?

The urethra is such an integral part of the prostate that it is impossible to retain it when the prostate is removed.

What can a man expect regarding surgery?

Radical prostatectomy is done under either general anesthesia, which puts the patient to sleep during the surgery, or under spinal anesthesia. The operation lasts from about 1.5 to four hours. Blood transfusions may be needed during and after surgery. Some hospital programs allow the patient to donate and store his own blood before surgery, for use during and after the operation. More recently, an attempt has been made to use medications to increase red blood cells (and the hemoglobin in red blood cells, which carries oxygen) in the body in advance so that transfusions can be avoided.

Most patients stay in the hospital for about three days after radical prostatectomy, followed by about 3-5 weeks recuperating at home. To assist with urination, a rubber catheter will stay in the penis and urinary bladder after surgery until the area is sufficiently healed. This is generally about two to three weeks, but may be longer.

What happens to the prostate and other tissues removed during the operation?

These are sent to pathologists. In their lab, the pathologists carefully slice the tissues, take samples, and determine:

- How large is the cancer?
- How many separate cancers (tumors) are there?
- Do the cancers involve only a portion of the prostate or the entire organ?
- What is the tumor's Gleason grade?
- Are the seminal vesicles invaded by the cancer? If so, on one side or both?
- Did the surgeon remove all of the cancer or leave some behind?
- How wide are the margins (edges of the prostate)?
- If the margins are positive (contain some cancer cells), is the involvement focal (limited) or extensive?
- Are the lymph nodes involved with cancer?

If the prostate has positive margins, there may still be cancer in your body, and additional treatments may be needed, such as radiation or hormones, or both.

How is the radical prostatectomy performed?

There are three approaches to radical prostatectomy: retropubic, perineal or laparoscopic. In the U.S., the retropubic method is the most common (over 90%). The surgeon makes an incision in the lower part of the abdomen. The approach is called "retropubic" because access to the prostate is made behind (i.e. "retro" as in retroactive) the pubic bone, which is the bone you feel in the area of the pubic hair. Retropubic surgery offers the surgeon easier access to the prostate and a better view of the nerves that make erections possible, which he or she will try to leave intact, if possible.

Perineal prostatectomy (performed in 8-9% of all RPs) is done through the perineum – the area between the scrotum and anus. Both surgical methods of RP can be equally effective. However, lymph nodes cannot be sampled during perineal prostatectomy. The perineal approach also involves less bleeding and offers heavier men an easier recovery. It has a shorter recovery time and thus may be preferred for older men.

The third type of radical prostatectomy, the laparoscopic, is performed only about 1-2% of the time. In a laparoscopic RP, the surgeon makes a tiny hole and threads a lighted tube and a scalpel through it, so there is a smaller incision and a shorter recovery time. Laparoscopic RP has been an option only since 1998 and even then only at selected cancer centers, so there is no long-term information on how well it works.

What are the side effects of radical prostatectomy?

The most common and bothersome side effects of radical prostatectomy are incontinence (inability to control urine flow) and impotence (inability to have an erection). These are major concerns, but you should keep in mind that, left untreated, cancer kills, and enduring these side effects is preferable to allowing the disease to progress. Thanks to recent advances in surgical techniques, fewer men experience these side effects.

The skill, experience and dedication of the surgeon will strongly influence whether or not there are side effects from RP. You want to go to a well-trained surgeon who performs the procedure regularly. Side effects occur less frequently when surgery is done at a major cancer center, where radical prostatectomies are performed routinely. It is also important for you to discuss with your doctor what you expect from the surgery, and compare this to what your doctor expects to occur. You may

have different ideas of what degree of urinary incontinence and impotence there will be, and how long it will take to resolve those side effects, for example.

Many of the side effects of surgery can also occur with treatment by radiation. The difference is that with surgery, incontinence and impotence occurs immediately, while with radiation therapy, these problems may appear gradually (incontinence is very rare with radiation, however). Managing side effects remains an issue for all patients regardless of the treatment they choose.

Most men will have problems having an erection in the first few months or more after surgery (it can take as long as 3-4 years for erections to return). Several patient characteristics influence whether or not side effects occur, and whether they are temporary or long-lasting. With respect to impotence, these variables include the patient's age, pre-operative potency, the extent to which the surgeon was able to preserve the nerve bundles during surgery, and the extent of the disease. Younger patients tend to rebound more readily than older patients and have a better chance to regain the ability to have erections after radical prostatectomy. After standard radical prostatectomy, 50-90% of men will be impotent (it varies with age). If a patient had a strong capacity to have erections before surgery, than there is a greater chance of regaining it after surgery. If patients were having problems with erectile dysfunction before surgery, then they are less likely to have the ability to have erections after surgery. (For example, about three-quarters of men over age 70 suffer from erectile dysfunction. This occurs naturally in all men, and also relates to health issues such as whether or not a man smokes, overuses alcohol or other drugs, uses multiple medications, has diabetes, cardiovascular disease, hypertension or multiple sclerosis, and other conditions. So, prostate cancer treatment will not adversely affect the potency of these men, and they may not be concerned about it.) If the surgeon was able to preserve both bundles of nerves that control erections, than the patient has a better chance of regaining potency. If only one bundle was preserved, the chance lessens. Of course, due to the surgeon's judgment during surgery, it may not be possible to preserve either of the nerve bundles. A surgeon's first priority—and yours—is getting all the cancer out. The last factor that affects potency is the extent of the disease. If the cancer is confined to the prostate, there is a better chance of retaining potency.

Keep in mind that what may be lost after radical prostatectomy is the ability to have an erection, and not your sex drive. For men suffering from impotence, there is still "sex" after surgery, though it may not be quite the same as before. Cer-

tainly, it will be less spontaneous. It is very important that you involve your sexual partner in deciding what you will do about sex. Fortunately, there are medicines and other treatments to help men achieve erections after surgery, such as Viagra (generic name sildenafil citrate), Cialis (tadalafil), and Levitra (vardenafil hydrochloride). Other aids include vacuum erection devices, injections, intraurethral therapy, and penile implantations. You should discuss these options with your doctor. I know this can seem embarrassing, but trust me, this is a common medical problem and your doctor has had many conversations about this with his or her patients and can help you.

Infertility is another side effect of surgery – loss of the ability to produce viable sperm. One other side effect is that following prostatectomy, there may be a shortening of the penis. This was first reported by patients and has since been verified by doctors. The reason for this shortening is unknown, though one theory is that it is due to removal of the prostatic urethra in the operation *(Munding MD, Wessells HB, Dalkin BL. Pilot study of changes in stretched penile length 3 months after radical retropubic prostatectomy. Urology. 2001 Oct;58(4):567-9)*. In one study, 68% of patients who had a radical retropubic prostatectomy had a decrease in penis measurements three months after surgery *(Savoie M, Kim SS, Soloway MS. A prospective study measuring penile length in men treated with radical prostatectomy for prostate cancer. J Urol. 2003 Apr;169(4):1462-4.)* Thus, patients should be advised before surgery that shortening of the penis might result.

With regard to incontinence, the other major side effect of radical prostatectomy, in most men continence returns sometime between a few weeks to a few months after surgery. You will be wearing absorbent underwear for some time after surgery. About one-third of all men undergoing prostatectomy will have minor bladder control problems permanently (these are things such as releasing small amounts of urine when laughing, coughing, sneezing, or exercising). In a few men (about 2-5% of all cases), more severe incontinence will persist after prostatectomy, perhaps permanently. As with other side effects, younger patients experience these less frequently and intensely. The skill of the surgeon is also very important. Your doctor will suggest several ways to improve your continence, including surgery, medicine, and Kegel exercises.

Besides impotence and incontinence, there are a few very rare surgical side effects of radical prostatectomy. The most common intraoperative complication is hemorrhage (excessive bleeding); other rare complications are injuries to the rectum or

ureter, myocardial infarction, pulmonary embolism and deep vein thrombosis. Death from the operation is extremely rare (all surgery involving anesthesia carries this risk). Possible complications after surgery include blood clots and bladder neck constriction.

One other "side effect" is depression. Depression is common among cancer patients. Speak to your doctor and family members about this, because depression should be treated. As you read through my description of possible side effects, some of which are worst-case scenarios, please do not imagine that these inevitably describe your future. They do not. Imagine instead that you have cancer as an interruption in your life, but after a period of time of managing it, you will get on with the rest of your life.

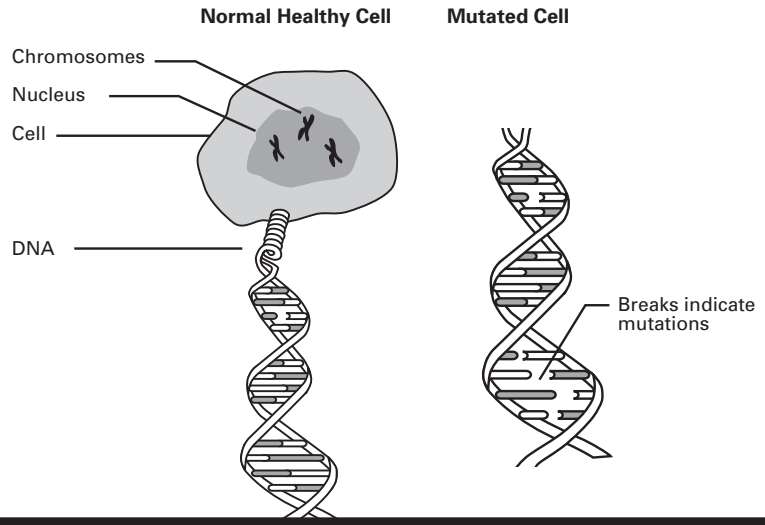
◆ Advanced Notes

Pathology Tests: Major institutions that have extensive experience with prostate cancer do "whole-mount" sections and computer planimetry. That is, the pathologist slices the removed prostate into many narrow slabs, like bread-slices, without cutting each slab into many pieces. Computer planimetry can determine the volume of the cancer and how many cancers are present in the prostate gland. However, one can get most of the information listed above without whole mount-sectioning and computer planimetry.

Radiation Therapy

The word "radiation" often brings trepidation. Radiation can heal, or it can destroy. X-rays have been tested and used for close to 100 years in the treatment of cancer. Technological improvements have made the use of x-rays safer and even more effective than ever before. In the hands of experienced physicians, radiation can heal. It is more difficult to understand how x-rays kill cancer cells than how surgery destroys cancer. With surgery, one cuts the cancer out and disposes of it. Things are more complicated with x-rays. X-rays work like invisible knives at the level of DNA [see Figure 13]. Many patients have a misconception that radiation is used only to slow the spread of cancer, and not to cure it. Still others mistakenly believe that radiation causes cancer, and can't understand how it could be chosen to cure cancer. Both radiation and surgery can be curative.

Figure 13a



DNA and Cancer Formation

DNA looks like a twisted double staircase. DNA is the basic building block of the genes, which carry genetic information from parents to offspring. DNA and genes control the activities of cells, including cell growth, function, longevity and cell death. Many cancers arise because of mutations — abnormal changes — in genes.

DNA gives out messages to produce specific proteins, which in turn carry out specific functions in the body. When DNA in some cells is damaged or malfunctioning, it sends wrong signals which stimulate these cells to multiply incessantly and out of control. This is a simple explanation of cancer formation.

X-rays create breaks in the supporting columns of the DNA's twisted staircase. If x-rays can break both columns – a "double break" – then the DNA "collapses" and the cell dies. However, if only one of the two columns is broken (a "single-strand break"), the cells may be able to repair the damage and survive. But the cell which had suffered a double break or an unrepaired single break in the DNA will die only when the cell tries to multiply again.

Figure 13b

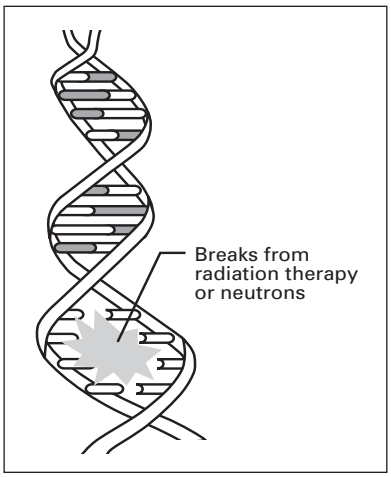


Table 6. Levels of Radiation

Diagnostic X-Rays	Radiation Therapy	Neutrons	Protons
Mild doses of radiation	Moderate to high doses of radiation	High doses of radiation	Similar to x-rays, but has specific "physics-related" advantages
Low energy Use: X-rays (e.g., chest x-ray, mammogram)	High energy Use: Treatment of cancers	Very strong energy Use: Treatment of special cancers (not for prostate cancer)	Very strong energy Use: Treatment of special cancers, including prostate cancer

In a biochemical sense, the cell may live, eat and breathe until it tries to make offspring. The damage from x-rays is immediate. However, the effects of x-rays are not immediate, but take time to manifest themselves.

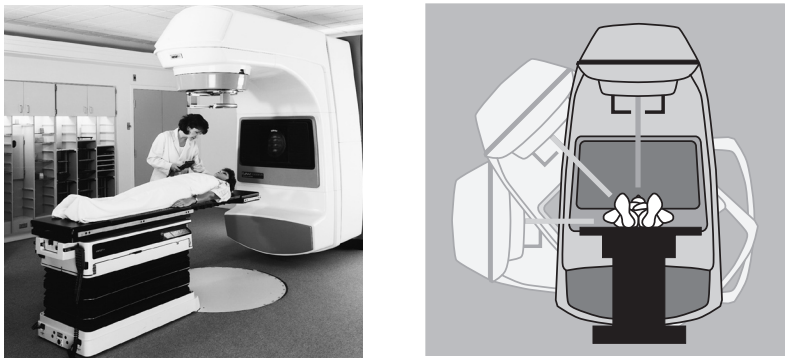
While radiation therapy has been used for some cancers for a century, it was not used in the treatment of prostate cancer until the 1960s. Prior to the '60s, radiation produced by then-existing machines was not powerful enough to reach the depths of the human body. The x-rays produced by these primitive machines gave more radiation dose to the skin than to the cancer. Some of the bad reputation radiation receives is based on this old experience. Fortunately, things have improved dramatically with x-ray treatments. Radiation has fewer side effects today when it is given therapeutically in controlled conditions, such as the use of IMRT.

You might be a candidate for radiation therapy (RT) if:

- You have early stage prostate cancer and want to be cured of the disease.
- You have advanced disease (the aim is to control your disease, shrink the tumor, and relieve pain).
- You wish to avoid surgery.
- You expect to live longer because of this treatment than you would if you left the cancer untreated.

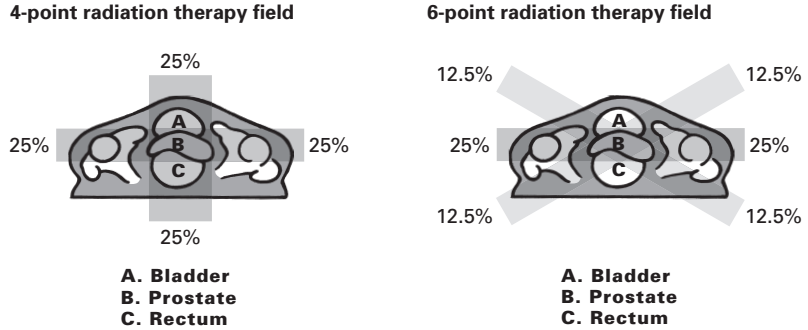
Note that patient age is no longer a consideration in whether someone can receive RT (in the "old days," most patients referred for RT were elderly – this is no longer true).

Figure 14



Shown above is a modern machine (circa 1999). This table — like modern four-way power car seats — can be moved up and down, to and fro, forward and backward, etc., precisely. The source ("gantry head") where x-rays are produced can move around the patient (180^0) and deliver the radiation from any desired angle (see right panel). (With permission from Scientific American.)

Figure 15



Many cancer centers deliver radiation therapy using four-point fields, which pass directly over the penis in front, the rectum in back, and through each side. Technologically more advanced centers deliver radiation using six-point fields. The six-point approach avoids delivering radiation directly over the penis and rectal areas, and therefore reduces the side effects to these organs.

How has today's technology improved radiation therapy?

The traditional method of radiation used to treat prostate cancer is external beam radiation therapy (EBRT), in which a machine outside the body targets a beam of radiation at the cancer cells. With modern technology, radiation therapy can:

- Give more dose directly to the prostate than to surrounding healthy tissues.
- Help physicians use x-rays to see the prostate and surrounding tissues in three dimensions, so that the radiation beams can be tailored more precisely to each individual patient's unique needs.
- Estimate what dose of radiation the nearby rectum, bladder and penis will receive during the course of x-ray treatments to the prostate.
- Safely provide a higher dose of radiation than even five years ago, which helps to improve the chances of cure. Improvements in radiation therapy make it impossible to compare the results of radiation studies done years ago with what is possible today—more advanced technologies and procedures are being used today.

How are doses of radiation measured?

Radiation is measured in units called "rad" or centigray. A typical dose of radiation given in a single treatment is 180-200 rad. These amounts are precisely calculated so as to destroy cancer cells and cause minimal damage to healthy cells.

What should I expect with radiation therapy? How is it given?

To understand radiation therapy, it's helpful to discuss the duration of treatments, the dose, preparation, side effects and complications of radiation therapy.

Duration of radiation treatments:

Radiation therapy is painless and does not make you radioactive. The actual procedure takes only a few minutes each day (though you need to allow about 30 minutes for each treatment session). Radiation therapy is given in small doses daily, usually for seven to nine weeks. It is usually given Monday through Friday, with weekends off. (Why not give the radiation dose in a single large "blast" and be done with it? This approach has been tried in the past, but caused too many complications.)

In general, the body has two types of healthy tissue, as far as radiation effects are concerned. I refer to these tissues as "short-tempered goodies" (STGs) and "long-memory chronics" (LMCs). The STGs are tissues that respond immediately after radiation treatment, manifest symptoms quickly, and settle down soon. Whether a patient receives 180 rad, 200 rad, 250 rad, or 300 rad per day (the usual range of doses given per day), the STG tissues respond to the radiation in about the same way.

The LMCs are different. These tissues show almost no reaction immediately; but after 6 months, 12 months or even 2 years, they manifest the effects of radiation. LMCs do mind how much radiation is given per day; the smaller the daily dose (usually 180-200 rad), the less damage the tissues manifest long-term.

In other words, the ill effects of radiation on normal tissues depend upon the following:

- The dose given per day.
- The total dose over time (that is, adding up all the daily doses to reach a grand total).
- How much volume of a tissue is being treated. (Example: *The chances of serious complications are greater if the whole rectum or bladder is irradiated versus irradiating only a portion of the rectum or bladder.*)

To avoid long-term problems and to improve the chances of a cure from cancer, radiation doses are given in small quantities nearly every day over a long period. Spreading out radiation doses also allows healthy cells to recover and survive.

Dose of radiation treatments:

There are a few numbers you want to remember if you are going to have radiation therapy for localized prostate cancer:

- The dose of radiation per day should be between 180 and 200 rad. (A higher dose of 250-300 rad may be given if cancer has metastasized.)
- Total dose over time = 6600 to 7400 rad (grand total) for localized cancer.
- Be sure to ask your doctor about these two numbers.

How does the doctor decide what dose to give?

That decision is based on experience, both the individual doctor's personal experience, and cumulative experience in treating hundreds of thousands of patients over decades by radiation oncologists.

Until very recently, the amount of total cumulative doses of radiation used to treat prostate cancer was based on how much radiation the rectum or bladder could withstand, rather than on the size of the cancerous tumor. Studies showed that, when less than 6000-6500 rad of total dose was given to patients with prostate cancer, the cancer often grew back; if more than 7000 rad was given, the rectum and bladder were hurt too much. Therefore, a dose between 6500 rad and 7000 rad was often chosen. That was true until a few years ago.

Today you need to know:

- Total doses higher than 7000 rad can be given more safely, thanks to newer, sophisticated techniques used by experienced physicians.
- Total doses higher than 7000 may, in fact, be more effective at controlling some cancers than lower doses of radiation.

Preparing for radiation treatments:

By "preparing for radiation treatments," we do not mean getting the patient and family prepared mentally. Instead, we are focusing on the steps necessary to make sure that appropriate radiation treatments are given. Many patients go through a three-step process:

1. Mold-making session.
2. CT scanning session.
3. Finalizing session.

These three steps are all focused on a single objective: hitting the target (tumor) as precisely as possible with radiation beams, while minimizing damage to healthy tissue that surrounds the tumor. The main targets are the prostate gland and seminal vesicles. As much as possible, we want to avoid nearby structures: the bladder, rectum, femurs (thigh bones) and penis.

What are the objectives of these three preparatory steps?

First, the physician must be able to visualize the targets, which are deep inside the body. Also, the prostate varies tremendously in size among men; so, the physician needs to know exactly how large it is in a given patient and where it is, and then decide how to strike the prostate with radiation. CT scans help us to see structures inside the body.

Second, the target is a moving target; that is, the prostate moves within the body from day to day. Minimal movement of the prostate will help assure more accurate positioning of radiation beams. It's also important to know how much movement occurs from day to day. Studies have given an estimate of prostate motion. Third, we don't want the patient to move during treatment; otherwise the radiation can miss the cancer target. Making a body mold helps to minimize movement by immobilizing the patient during treatment.

Finally, we want to shape the radiation beam so that doses to the rectum, bladder and penis are minimized.

The three-step preparation process is essential for achieving all of the above objectives.

How do these steps achieve the objectives?

A personalized mold is made so that the patient will be in the exact same position from day to day while receiving radiation treatments, and so that he will not move when the radiation beam is on. The mold is a thin sheet of plastic that softens when put in boiling water and is then wrapped around the body. When the plastic cools, it hardens and will retain its shape – the precise shape of that particular patient. The personalized mold is attached to the treatment table so the patient remains in the same position and cannot move during treatment. [Figure 16]

A CT scan is done to see the location of the target – the prostate and seminal vesicles – and the rectum, bladder and penis. The CT scan is done with the mold in place.

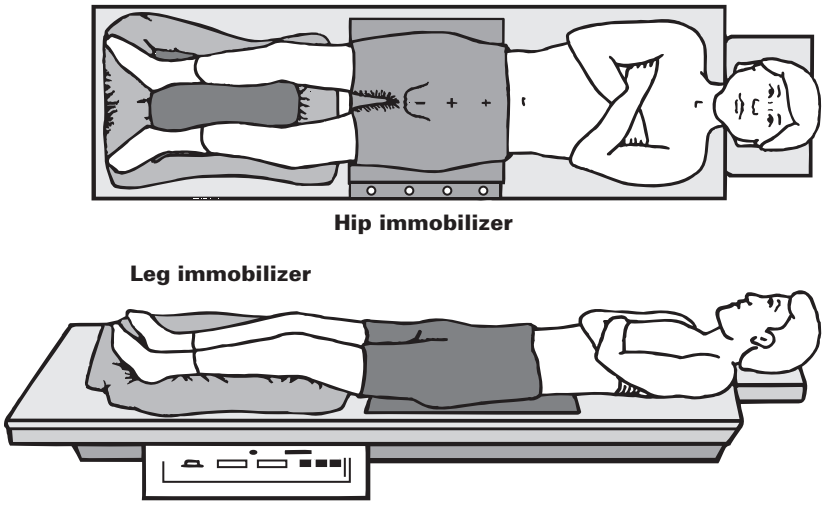
Once a personalized treatment plan is designed based on the above two steps, the final dry run, mock session is conducted. This is referred to as a "simulation." This enables the physician to rehearse the precise positioning of radiation beams for each particular patient, before actual radiation therapy begins.

Your radiation oncologist will have further information on treatment procedures and how you prepare for them (the next few pages discuss IMRT and BAT, for example). For example, you will be asked to have a full bladder before each treatment, so that your prostate is held in the same place each time. You will also have tiny ink marks tattooed on your skin to help the radiation therapist aim the beams correctly each time. You will also have custom-made "shields" to protect vital body areas from scattered rays.

The general pattern for radiation therapy treatments is to first have five to six weeks of radiation to a wider area so as to kill any cancer cells that have gotten to any surrounding tissues (for example, seminal vesicles). Next, the beams are aimed directly at the prostate, giving your intestines and bladder as low doses as possible.

In fact, treatments are often designed more precisely based on your individual prognostic factors. In my practice, patients in Group I – those who are T_1-T_{2b} and Gleason sum ≤6 AND PSA ≤10, which is a favorable prognosis – generally receive radiation to the prostate only. Group II – those who are T_{2c} or Gleason sum =7 or

Figure 16



Examples of Immobilization Techniques
One example of a personalized mold are the hip-immobilizer and the leg-immobilizer as illustrated here. More modern ways of assuring day-to-day reproduction using video cameras are currently being investigated.

PSA between 10 and 20 – will most likely receive radiation to the prostate and the proximal seminal vesicles as well for the first 5-6 weeks, followed by a "boost" to the prostate. Group III patients – having more than one of the above three factors with a higher value – receive radiation therapy to the pelvic nodes and seminal vesicles for the first 5-6 weeks, followed by a "boost" to the prostate. Group II and III patients often receive adjuvant hormonal therapy.

Today new equipment and techniques have been created to make radiation therapy more precise than ever – two of these are IMRT and BAT. Another new treatment involves leaving some non-radioactive seeds in the prostate and monitoring them. The reason for these new techniques is that the prostate moves ever so slightly each day, head to toe, back to front, and left-right (1-3 mm.).

What is IMRT?

IMRT is short for Intensity-Modulated Radiation Therapy. This is the newest and most precise way of delivering radiation treatments. It is another form of external beam radiation therapy (EBRT).

How is IMRT different than conformal radiotherapy (CRT)?

Although both CRT and IMRT make use of a planning scan, usually a CT scan, there are two main differences:

The first is in the way the treatment planning is done – with IMRT, the planning is done using sophisticated computer software that tries to shape the radiation dose to what the radiation oncologist specifies.

The second is in the way the treatment is delivered – whereas during CRT the radiation coming out of the machine is uniform and uses a single beam of radiation, with IMRT there are as many as 80-120 sliding metal leaves that are used to shape the beam to fit the specific shape of each patient's prostate, and IMRT uses thousands of tiny beams ("beamlets"). These metal leaves also block radiation from getting to nearby healthy tissue.

What will be done differently (than with CRT) at the time of treatment?

The radiation beam will be directed at the prostate region from several different angles, as they would for CRT. However, there may be more or fewer angles depending on your treatment plan. Overall, IMRT may require a few more minutes on the treatment table per day than CRT (approximately 25-30 minutes, compared with 20-25 minutes), due to the improved shaping of the beam.

What are the advantages of IMRT?

IMRT allows for shaping the radiation dose more precisely to avoid more of the surrounding bladder and rectum, compared to CRT. Some studies have gone further to show that the side effects, particularly the rectal side effects, can be reduced over those expected with CRT. Finally, depending on your particular treatment plan, your radiation oncologist may feel comfortable going to a higher dose to the prostate over that which could be done safely using CRT.

What is the BAT?

BAT is short for B-mode ultrasound Acquisition and Targeting system. This is a fancy way of saying that the prostate will be tracked daily during the radiation

treatments. The BAT can be used with either conformal radiotherapy (CRT) or intensity-modulated radiotherapy (IMRT).

What does the BAT involve?

During the treatment there is a machine that has an abdominal ultrasound probe that is put over the lower abdomen to see the bladder, prostate, and rectum on the day of treatment. Please note that this is not an ultrasound probe that goes through the rectum but rather, one that is pressed on the skin. The radiation therapist uses this probe daily to see the bladder, prostate, and rectum so that the table can be adjusted slightly to match the position of the prostate on the day of treatment. Because the ultrasound images are better with a full than with an empty bladder, you may be asked to drink water before your daily treatments. The BAT system requires you to be on the table a few minutes more than without and allows the treatment to be delivered more precisely to the prostate.

What is the advantage of the BAT?

Studies have shown the ability to track the prostate more precisely with the BAT than without, and BAT allows the radiation oncologist to aim better at the cancer.

What are the advantages of radiation therapy?

The advantages of radiation therapy are that it can cure localized prostate cancer just as effectively as surgery and can control more advanced cancer, where surgery would be ineffective. It is easily administered on an outpatient basis, allowing patients to maintain their normal work schedules while receiving treatment. Surgery and anesthesia are avoided. Finally, there is no immediate incontinence or erectile dysfunction.

How will I know if the radiation worked?

Radiation therapy's effectiveness is measured using a 'PSA nadir,' which is the lowest point of the PSA after treatment. Most men who achieve a PSA nadir are cured (for example, a nadir of 0.2 ng/ml after radiation therapy for prostate cancer--though your nadir will be determined by your doctor and may be higher). The time it takes to achieve a nadir is different for each patient: while the nadir can occur as soon as three months after treatment, it generally occurs two or three years after radiation therapy. The PSA should then stay at that low level. If PSA starts to rise again, a recurrence of cancer is said to have happened if there are 3 consecutive rises spaced over a period of about 18 months. However, if a patient has BPH too, doctors will look at the stability of the PSA, and not just at whether or not it is at

a low level. The other concerning factors are the rate of PSA rise (PSA doubling time) and the absolute rise in PSA.

What are the common side effects from radiation therapy?

First, it is important to understand the difference between "side effects" and "complications." Side effects are problems caused by the treatment that can be managed in some way while treatment continues (though the emergence of some side effects might lead to treatment changes). Often, side effects last for only a short period of time. For example, the side effect of having dry skin caused by radiation treatment can be managed by applying an appropriate lotion. Complications are medical problems that arise in addition to a patient's original problem; they are more severe than side effects because they require that changes be made in your treatment. Complications are generally unexpected, whereas side effects are anticipated.

Now that you know what I mean by "side effects," let's discuss them. The most common major side effects from radiation therapy are bowel problems, urinary problems and impotence. Additional minor side effects include dry skin, loss of appetite and decreased energy. These will diminish after a few months. These complications can be mild or severe, and short- or long-lasting, and vary greatly depending on the skill of the radiation oncologist. About 60 to 75 percent of patients will experience only minor side effects. It generally takes at least a few weeks for the side effects of radiation therapy to appear, though some can develop months later. Newer radiation therapies, such as conformal beam imaging and IMRT (discussed a few pages ago), give patients fewer bowel and urinary side effects.

Because the bowel is located so close to the prostate, it is common to have bowel-related problems after treatment with radiation therapy. These problems can vary widely in severity and include diarrhea, blood in the stool, rectal itching, constipation, a sense that you urgently need to have a bowel movement, and painful cramps. Most bowel disorders improve on their own. However, a small percentage of men suffer permanent rectal damage after radiation therapy. Doctors can offer treatments for bowel problems with medications and by suggesting diet changes tailored to each patient's particular problem.

Urinary problems of some sort occur in about three-quarters of men treated with radiation therapy, and can include feeling as if you urgently need to urinate, painful urination, urine leakage, and the need to urinate frequently, especially at night. There are medicines that your doctor can prescribe to help manage some of these problems.

Impotence (inability to get an erection) due to radiation is thought to be caused by radiation's damage to the nerves that control erections and to the blood vessels in the penis. Impotence develops gradually after treatment, sometimes over a period of years. About half of the men who could have erections before treatment retain that ability after treatment (a few of my papers discuss this issue: see the Mantz 1999 and Mantz 1997 references at the end of this book). However, for other men impotence can be a permanent side effect. As with surgery, younger patients and those able to achieve erections before treatment have a better chance of retaining the ability to have erections after treatment. Remember that there is a natural age-related decline in potency in men. Also, the more advanced the stage of prostate cancer, the less likely it will be that potency can be retained after treatment. Smokers, patients with diabetes, hypertension, and/or vascular disease are more likely to have problems achieving erection after radiation therapy. As with surgery, there are medications (such as Viagra) and other aids that can help some men achieve erections after treatment. Even without erections men can still have a sex life.

Depression will occur in some men who have had radiation treatment, just as it will for some men who undergo surgery to treat their prostate cancer. For this, please seek out family, friends, and professionals who can help you manage your emotional well-being. It is easy to become so caught up in trying to manage the physical aspects of your disease and recovery from treatment that you forget to tend to your psychological and spiritual health.

Watchful Waiting

Some patients are perturbed, even shocked, that one of the standard treatment options for prostate cancer is no treatment at all. Physicians call this approach "watchful waiting." Watchful waiting is not quite the same as doing nothing, nor should it be associated with either a painful or certain death. Although the patient is not being actively treated, he continues to be monitored regularly by his physician, to identify any signs that the cancer is worsening. Most likely you will see your doctor every 6 to 12 months and report any new symptoms at those visits. If the cancer worsens, the physician and patient may decide to pursue a different treatment course (such as hormonal therapy).

When watchful waiting is suggested, patients often ask:

Do I have cancer?	(Yes.)
Doesn't cancer spread?	(Yes.)
Doesn't cancer kill?	(Yes.)
They, why no treatment?	

The answer to this series of questions is complicated. Whether no treatment is in fact a "treatment" for men with prostate cancer depends on the following facts:

- We will all die someday, hopefully later rather than sooner.
- Prostate cancer generally grows slowly.
- Prostate cancer most often affects men over 60 years of age, whose life expectancy is shorter than a younger man.
- Men over age 60 often have other medical problems such as heart disease, diabetes, or stroke. These other conditions are as dangerous and, sometimes, cause death even swifter than prostate cancer would. In other words, a man with prostate cancer may be more likely to die from another cause of death before the prostate cancer would cause death.

Therefore, if a man has prostate cancer that is growing slowly and spreading slowly, and if he has other severe medical problems that are more life-threatening than prostate cancer, then it is reasonable to give no immediate treatment to the prostate cancer as long as no problems have occurred.

Some patients may prefer to postpone treatment, even if they don't have significant medical problems other than prostate cancer. This is because the complications of treatment (surgery, radiation therapy or hormone therapy) are often immediate or occur within one to two years. On the other hand, the complications and problems of untreated, slow-growing prostate cancer may not occur until five to 10 years after diagnosis.

However, do not be tempted into choosing watchful waiting if you are in your 50s or 60s and in good health. First, because you are young, the cancer will have many years to grow. Second, it is easy to imagine the first pleasant period of watchful waiting, when you are avoiding the complications and side effects of treatment, and forget about the later period when you could be living with advanced cancer. Do not choose watchful waiting if you are doing so simply to delay therapy. The

quality of life benefit you are seeking will be only temporary. If you have a chance to cure your cancer now with definitive treatment, do so.

What are the disadvantages of watchful waiting?

- The cancer can spread to the bones, lungs or other organs as we are waiting.
- The local growth of the tumor can cause symptoms, especially urinary symptoms.
- Some men experience a psychological anxiety of living with cancer yet not treating it. The cancer will not disappear without treatment.

What are the benefits of watchful waiting?

- The unpleasant aspects of cancer treatment are avoided. Treatment inconveniences (such as making time daily for radiation therapy) also are averted.
- Potential side effects and complications – such as incontinence or impotence – are avoided.
- Money is saved: by the patient and by insurers.

Which patients are potential candidates for watchful waiting?

- Patients with early-stage, slow-growing cancer (T_1 or T_2).
- Patients with low-grade cancer (Gleason Score less than 5-6).
- Patients with low PSA levels (less than 10-15 ng/ml).
- Men age 70 or older.
- Patients with many medical complications, such as heart attacks, previous bypass surgeries, strokes, uncontrolled heart failure, and other such problems.

Watchful waiting is a personal and personality-dependent decision. If a patient fears the treatment and its complications more than he fears not being treated, if he thoroughly understands the implications of watchful waiting, and if he meets the five criteria above, he may be a good candidate for the watchful waiting approach to prostate cancer. However, remember: it is watchful waiting – not just doing nothing. A man with prostate cancer still needs close follow-up by an experienced doctor. Your doctor most likely will follow-up every six months or so with DREs, PSA tests, and, very rarely, biopsies (biopsies are generally done only under experimental conditions, when a patient is enrolled in a clinical trial).

Chemotherapy and Alternative Treatments

Is chemotherapy a standard treatment for prostate cancer?

No. At this time, there is no effective chemotherapy for prostate cancer because current chemotherapy does not kill enough of the prostate cancer cells to effectively destroy the disease. Chemotherapy is toxic to healthy cells as well as cancer cells, which leads to many side effects (side effects vary widely and depend on the patient's age and general health, the spread of cancer, the medications being used, and their strength; examples of side effects are nausea, vomiting, hair loss, loss of appetite, and gastrointestinal bleeding). However, chemotherapy can be effective in treating many other types of cancers.

There is one type of advanced prostate cancer for which chemotherapy can be used instead of hormonal therapy – small cell carcinoma. This cancer most often develops in the lungs, but when it occurs in the prostate, chemotherapy (cisplatin and etoposide) can treat it.

Even for metastatic prostate cancer, chemotherapy is generally used only after the body has stopped responding to hormonal therapy. Chemotherapy can reduce pain and slow tumor growth, but it does not destroy all of the cancer cells. However, several promising drugs have emerged in the past few years. Some of the chemotherapy drugs used to treat prostate cancer are doxorubicin, estramustine, etoposide, mitoxantrone, vinblastine, paclitaxel, and docetaxel. Often two or more drugs are used in combination.

One FDA-approved chemotherapy drug currently in clinical trials is Paclitaxel (Taxol), which can be injected into the veins either alone or in combination with other drugs. Paclitaxel slows or stops the growth of cancer cells in your body. It is given to patients with advanced, androgen-independent prostate cancer (as well as other types of cancer). Ask your doctor if you might be a candidate for a clinical trial with this or other drugs.

What about alternative therapies?

If you want to try an alternative or unproven therapy, please let your doctor know because there may be unwanted side effects to your alternative therapy, or effects that interfere with the standard therapy you are receiving. You should conduct some research about your alternative therapy, such as by requesting information

from organizations like the American Cancer Society or the National Cancer Institute. If your alternative therapy causes you no harm, I see no problem with your pursuing it while continuing with your proven therapy.

Chapter 6

Advanced Treatment Options

Newer Approaches to Standard Therapies

Within the past 20 years, there have been several major clinical and technological advances that have created new options for treating prostate cancer. These advances include:

- PSA blood test.
- Transrectal ultrasound (TRUS), a test with which one can see the inside of the prostate well.
- Nerve-sparing prostatectomy.
- Three-dimensional conformal radiation therapy.
- IMRT

These five advances have changed the way we think about and deal with prostate cancer at many levels: (a) at an individual level in terms of treatments recommended to patients; (b) in dealing with prostate cancer as a national health problem; and (c) in terms of public-policy issues.

In this chapter, we are going to focus on the patient's point of view. Newer, advanced treatment options for patients with prostate cancer include:

- Nerve-sparing prostatectomy.
- Conformal radiation therapy (including proton beam therapy)
- Radioactive seed implant therapy ("brachytherapy")
- Cryotherapy

Nerve-Sparing Prostatectomy

Again, the words explain the meaning. Nerve-sparing prostatectomy is a type of surgery in which the prostate gland is removed while the nerves are preserved. The chance of impotence is much lower with nerve-sparing prostatectomy (though there is no guarantee that potency will be preserved). At one time, this was a relatively new procedure and not all surgeons practiced it. Today, it is the standard operation for radical prostatectomy (see Chapter 5). Be sure to ask if this is the type of surgery you are getting (if you have chosen surgery). Surgeons will also try to spare muscles that control urination, improving a patient's chances of retaining continence.

Which nerves are preserved, and why?

Let us look at a little bit of history to answer this question. Surgical prostatectomy is not new: this operation has been around for decades. In the past, one consequence of prostatectomy was taken for granted: sexual impotence. With the standard form of radical prostatectomy surgery, impotence occurs in more than 90% of patients because critical nerves are severed. There are nerves which are located only millimeters away from the prostate, on both the left and right sides, behind the prostate and in front of the rectum, which innervate the penis by sending nerve signals between the brain and penis. If the surgeon cuts through these nerves, sexual potency also is cut off. In a sense, cutting the nerves is like cutting through the electric wire between an outlet and light bulb.

In the newer nerve-sparing procedure, these critical nerves are preserved. A surgeon experienced in doing this more exacting surgical technique carefully avoids cutting the nerves off on both sides, or at least on one side. For 50-90% of patients, successful nerve-sparing prostatectomy leaves sexual potency intact.

Which factors influence the success of nerve-sparing prostatectomy?

- Age. Younger men fare better than men over age 68. The impotence rate is about 25-30% for men under 60 after nerve-sparing prostatectomy and 70-80% for men over 70.
- Location of the tumor within the prostate. If cancer is located close to the nerves, the nerves will have to be sacrificed. Also, if cancer is on a single side of the prostate rather than both sides, nerves can be spared on at least the non-cancerous side.

- Stage. If the cancer is Stage T_3 (Stage III/C), and has invaded the prostate capsule (the covering of the prostate), the chance of sparing these nerves is low.
- The surgeon's expertise. The experience and skill of the surgeon are perhaps the most important factors influencing the success of nerve-sparing surgery. This is a very delicate procedure that requires great precision from experienced hands.

What is the downside of nerve-sparing prostatectomy?

In the interest of sparing the nerve and sustaining sexual potency, some cancer may inadvertently be left behind in the body. Thus, the entire purpose of a prostatectomy—eradicating the cancer—would not be achieved. If cancer is left behind, one may end up needing radiation treatments in addition to surgery. It is usually preferable to have only one kind of major treatment: surgery or radiation therapy.

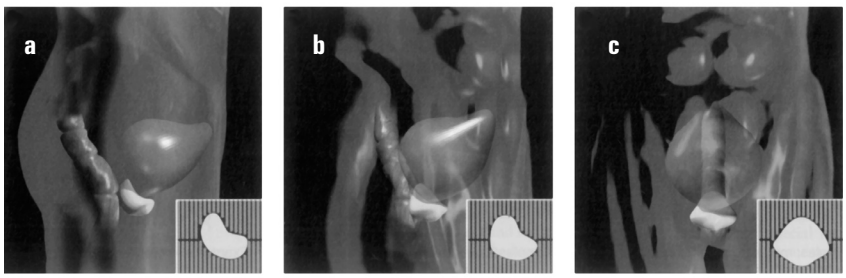
Conformal Radiation Therapy (CRT)

Conformal radiation therapy ("CRT") is a more advanced form of radiation therapy, and is today the preferred method when using radiation to treat prostate cancer. (The previous chapter discusses the most advanced form of CRT, called IMRT, and compares the two.) As with other radiation therapies, treatments last several weeks, usually being given on weekdays, with weekends off. The actual treatments last about 5-10 minutes.

This form of radiation treatment incorporates a three-dimensional reconstruction of the human body and its relevant inner contents: the prostate, bladder, rectum and penis. This three-dimensional imaging is provided with the aid of computers. [Figure 17] "Conformal" implies conformation of the radiation doses to the target (the prostate). In a sense, the radiation beam conforms to the individual's body structures (like a custom-tailored suit fits its wearer). In standard radiation therapy, the radiation beam is not conformed to the individual, but is more like an off-the-rack suit that fits a bit too loose or too tight.

Old radiotherapy can be compared to fitting square pegs in round holes. Conformal therapy is like round pegs that fit nicely into round holes.

Figure 17



In Figure 17, panels a, b and c are views 'seeing through' [meaning muscles and skin are removed using computer programs] the body from three different angles at the man's pelvic area. Left of each panel is the front of the body. The insert within each panel shows the prostate [white area within the vertical lines]. **Note that the shape of the prostate looks different from different angles. Conformal therapy enables the x-ray beams to target the prostate from different angles, similar to what is shown here. This facilitates precision and helps to focus radiation beams, avoiding the rectum, bladder, etc.** (With permission from Scientific American.)

How does conformal therapy help in prostate cancer treatment?

Three-dimensional conformal radiation therapy offers two significant advantages: It allows us to hit the target (prostate and seminal vesicles) with better precision than before; and it decreases the dose of radiation exposed to normal tissues. Therefore, we can more safely give higher radiation doses directly to the cancerous area, with less damage to surrounding non-cancerous tissue. Being able to safely give higher doses of radiation is important because higher doses have better success rates of curing prostate cancer.

Treatment planning is the key to CRT and begins several weeks before your first treatment. During this time, technicians will create a sort of body cast (a mold) fitted just for your body shape and your radiation oncologist will design a treatment plan specifically for you based on the three-dimensional map he or she creates of your pelvic region. Part of this treatment planning includes placing small tattoos on your body to help your radiation oncology team aim the radiation. During your treatments, you will wear this body mold to keep you from moving, so that high doses of radiation can be directed from several directions at just your prostate, which will be in the exact same position every time.

Why couldn't this be done before?

Before the advent of high-powered computers which enable us to see things inside the body in three dimensions, physicians could only estimate the exact size and shape of the prostate.

Three-dimensional reconstruction allows physicians to "see" the prostate and other structures more clearly. Three-dimensional imaging is like having your vision tested. You are given some glasses to put on and you are asked: "Do you see?" You say, "yes, but not that well." The eye doctor adds another set of lenses and you say with excitement, "Now I see clearly." With the new computer programs, physicians and technicians are able to see things much better, more clearly than before, and in three dimensions. But remember:

- Not all cancer doctors or medical centers have experience with conformal therapy.
- This is a relatively new technology which most people would consider as standard now.
- Conformal therapy is unlikely to harm you when administered by experienced hands, especially when radiation doses are the same as with the standard radiation therapy.

- Conformal therapy requires necessary software and experts who are familiar with this use of computers. You are most likely to find conformal therapy at academic medical centers, which tend to offer the newest promising techniques earlier. This technology is also available in many community hospitals.
- Some medical centers can give higher doses with conformal therapy than with the older, standardized radiation therapy. This may help to better control the spread of cancer.

What about proton beam therapy?

Proton beam therapy is a type of conformal therapy. It uses protons instead of x-rays. (Protons are part of atoms, and kill cancer without causing much damage to surrounding tissues, which enables higher doses of radiation to be delivered. Charge-sensitive protons pass through healthy tissues without causing damage, and can be stopped suddenly, so that they destroy cancer cells, but do not damage healthy cells beyond that point.) Currently, there are only two centers in the U.S. that have this type of radiation beam available for proton beam therapy, but more centers are opening. No direct comparisons have been made on the effectiveness of 3D x-ray therapy or IMRT versus proton-based treatment.

What are the side effects of 3D-CRT?

The good news is that side effects are lower using 3D-CRT, compared to conventional external beam radiation therapy, because radiation oncologists are better able to spare the healthy tissue from radiation. Side effects include:

- Mild to moderate urinary side effects, treatable with medications when necessary, lasting 6 weeks at most
- GU toxicity
- Impotence (13-29% incidence, lower than with EBRT)
- Bowel complications (10-34%, lower than with EBRT)

Which patients should benefit the most from 3D-CRT?

The same group of patients that might choose surgery, external beam radiation therapy, or brachytherapy is the one that can choose 3D-CRT – patients with early stage, organ confined disease).

Radioactive Seed Implant Therapy

Also called "brachytherapy," radioactive seed implant therapy puts radiation right where the cancer is ("brachy" is the Greek root for "short distance", and in this treatment the radioactive seeds are placed close to or directly in the tumor). Your radiation oncologist and urologist work together to perform this procedure. Up to 125 tiny radioactive seeds (about the size of a sesame seed) are implanted into the prostate and left there, while the radiation kills the cancer cells over a period of a few months. How long the seeds remain radioactive depends on the radioactive material used and its dose. The seeds can safely remain in the prostate for the rest of a person's life. These seeds are so small that patients do not feel them. The radioactive isotopes used are iodine or palladium.

What are the advantages of radioactive seed therapy?

Because the seeds are so close to the cancer cells, the cancer cells get inundated with radiation while the rectum, bladder, penis and other tissues generally receive minimal radiation. With seeds, a higher equivalent radiation dose may be delivered to the prostate than with external beam radiation.

In contrast, other radiation therapy techniques, including conformal therapy, penetrate radiation from outside the body to the inside; thus, the radiation must first go through normal tissue before it reaches the prostate located deep inside the body. With seed implant treatment, radiation hits the prostate first, and only then strikes normal tissues, when the radiation has weakened.

Is seed implant therapy a new technique? Why has it become more common in recent years?

Implant therapy is not new; the technique has been around for decades. However, advances in imaging technology have made implant therapy more effective.

Again, what was described under conformal therapy is true for implant therapy. Before computers enabled us to see inside the body, doctors could only estimate where a man's prostate was and where the radioactive seeds should be implanted. Thus, early results with implant therapy were not good and the approach was abandoned for years. Then came TRUS (transrectal ultrasound) that enables us to view the prostate more clearly. Using ultrasound to see the prostate gland better, physicians can place each seed in the prostate more carefully. With ultrasound-

guided radioactive implantation by very experienced physicians, recent results have been excellent. Computed tomography is also used.

Who should consider radioactive seed implant treatments?

- Men with very-early stage prostate cancer.
- Men with low-grade cancer.
- Men with PSA levels below 10 ng/ml.
- Men for whom sexual potency is very important, because seed implant therapy generally preserves potency better than some other therapies.
- Men with a prostate size of less than 50-60 cm. (small to medium-sized prostates). With large prostates, more seeds are needed to treat the whole prostate gland and so there is a greater chance of side effects.

What is the downside to consider?

Using radioactive seed implants creates a dilemma. Because vital structures in this area of the body are so close to each other, it is difficult to affect one part without also affecting neighboring structures.

Imagine the prostate, rectum and bladder as three rooms next to each other, with a common wall between them. To treat cancer in the prostate one has to put the seeds very close to the wall between the rectum and prostate, and the wall between the prostate and bladder. If the seeds are not close to these walls, the cancer may not be adequately treated. If the seeds are too close to these walls, the rectum or bladder may receive high doses of radiation. [Figure 18]

Figure 18

A. Bladder B. Prostate C. Rectum

The drawing on the left shows an example of radiation seeds placed too close to the bladder (A), and rectum (C) which causes the bladder and rectum to receive high doses of radiation. The drawing on the right shows proper radiation seed placement so that only the prostate is treated with radiation. The possibility of some cancer cells not getting a sufficient dose also exists.

A few other points should be considered.

- Seed implantation is a type of surgery. Needles are inserted into the prostate through the patient's perineum (between the scrotum and anus). Therefore, just as in any surgery, the results depend upon the experience and skill of the operators: the radiation oncologist and urologist. This is considered minor surgery, generally uses local or regional anesthesia (though sometimes general anesthesia is used), and is usually performed as a one-day, outpatient procedure, with little time needed for recovery, or disruption of normal work or other activities.
- Like conformal radiation therapy, the modern ultrasound-guided implant therapy is new, and practitioners are still learning or perfecting their techniques. Long-term results are not yet available at many institutions. However, numerous studies have shown that 5-year recurrence-free survival rates with brachytherapy are the same as with radical prostatectomy or external beam radiation. (This makes selecting a treatment a difficult and personal choice.) Early reports on brachytherapy had many treatment failures because the techniques for seed placement were still being learned, and are not applicable to the procedure today.

Combining conformal therapy and seed implants to give a boost dose makes sense in theory. However, this combined approach has not been widely tested or documented. You may want to discuss combining therapies with your cancer physician team.

What are the side effects of brachytherapy?

- Fatigue after the procedure
- For a few weeks to up to two months, because you are mildly radioactive, you will need to avoid being close to children and pregnant women. Although the seeds continue to emit radiation for some time, most of the dose is absorbed by the surrounding tissue and very little penetrates the body. Nevertheless, as a precaution, you should minimize close contact with children and pregnant women.
- Urinary symptoms immediately after implantation, such as urinary retention, urgency and frequency, due to swelling from the procedure. This is only temporary.
- Impotence in up to half of men treated (this occurs gradually) – the incidence is less than with either radical prostatectomy or external beam radiation therapy. Products like Viagra can help treat this. How potent a patient is before the treatment affects potency afterwards.
- Bowel problems immediately after the procedure, such as diarrhea, cramps, rectal pain and burning (severe bowel problems are rare and occur less frequently than

with external beam radiation). Up to 5% of patients may have more permanent bowel side effects (burning, pain and diarrhea).
- About 10-15% of patients will require catheterization after the procedure.

How will I know if the brachytherapy is working?

Your doctor will monitor your PSA levels, which should reach their nadir (low point) and stay there. If your PSA has three consecutive rises over an 18-month period, then that is considered treatment failure (the same as with external beam radiation therapy). This definition of PSA progression is from the American Society of Therapeutic Radiology and Oncology (ASTRO).

Alternative definitions of treatment failure exist and may be applied to your treatment; Dr. Jani and I, with others, developed a prostate-specific antigen (PSA)-based definition of treatment failure (see references, Jani et al.), rather than just tracking PSA rises. Waiting for three rising PSA values may be too stringent when two large consecutive rises clearly indicate treatment failure or when the interval between determinations is long. Our nadir definition correlates more closely with clinical outcomes than the standard ASTRO definition.

Not all rises in PSA mean there has been treatment failure. A transient rise in the PSA has been known to occur between 1-3 years after brachytherapy and is known as "PSA bounce." The PSA level should subsequently decrease. You should discuss this matter with your physician.

Isn't there another kind of brachytherapy?

Yes. Besides standard brachytherapy, in which the seeds are left in the patient, there is also "high-dose-rate brachytherapy," in which the seeds are taken out after each treatment session. Usually this is done in combination with external beam radiation. This "temporary" brachytherapy is performed at only a few medical centers in the United States. High-dose-rate brachytherapy is for men with more advanced cancers that extend just beyond the prostate; high-activity iridium-192 is the radioisotope used.

Cryotherapy

Cryotherapy involves freezing tissue. In the movies and science fiction, cryotherapy is sometimes associated with cryopreservation, in which people are frozen to be thawed and brought back to life decades later.

In fact, cryotherapy (sometimes called cryosurgery or cryoblation) can be used to kill cancer cells, rather than to preserve them. Cryotherapy is performed on patients with early stage prostate cancer, when it is still confined to the prostate. It can also be considered in the event of radiation treatment failure (this is known as salvage cryotherapy, and is typically combined with hormonal therapy).

How can cryotherapy be used to kill cancer cells? Won't the cancer cells be preserved rather than killed?

The difference is in the detail; it depends on how cold the cancer gets. If you cool the cells to very low temperatures, for example -190°C, the cells will die. That is the principle of cryotherapy, which is performed by urologists under general or regional anesthesia.

In cryotherapy, metallic probes are inserted into the prostate gland through the perineum (there is no abdominal incision), using ultrasound guidance. Argon gas is sent through the rods and into the prostate, rapidly freezing the prostate and surrounding tissues (heat is applied to the urethra to prevent it from being frozen too). The cancer cells are destroyed when they start to thaw. The procedure, done as an outpatient or with a 1-2 day hospital stay, takes at least an hour and recovery takes 1-2 weeks. PSA levels will decline gradually after cryotherapy and success is measured by PSA nadir (reached after about three months), as with radiation therapy.

Cryotherapy made a big splash in the late 1980s and early 1990s. It seemed to be a procedure with a shorter recovery time than surgery and one with fewer complications, and it was believed that if it didn't work it could be repeated again, or patients could still choose to have radiation or surgery. Since then, it has faded in popularity because of conflicting results from the pioneers who first used cryotherapy for their patients. Some have achieved good results and low complication rates; others have had poor results and high complication rates. Again, some of these results may have depended on the skill and experience of the physician. Men with

large prostate glands should not choose cryotherapy because a prolonged freezing time will be required.

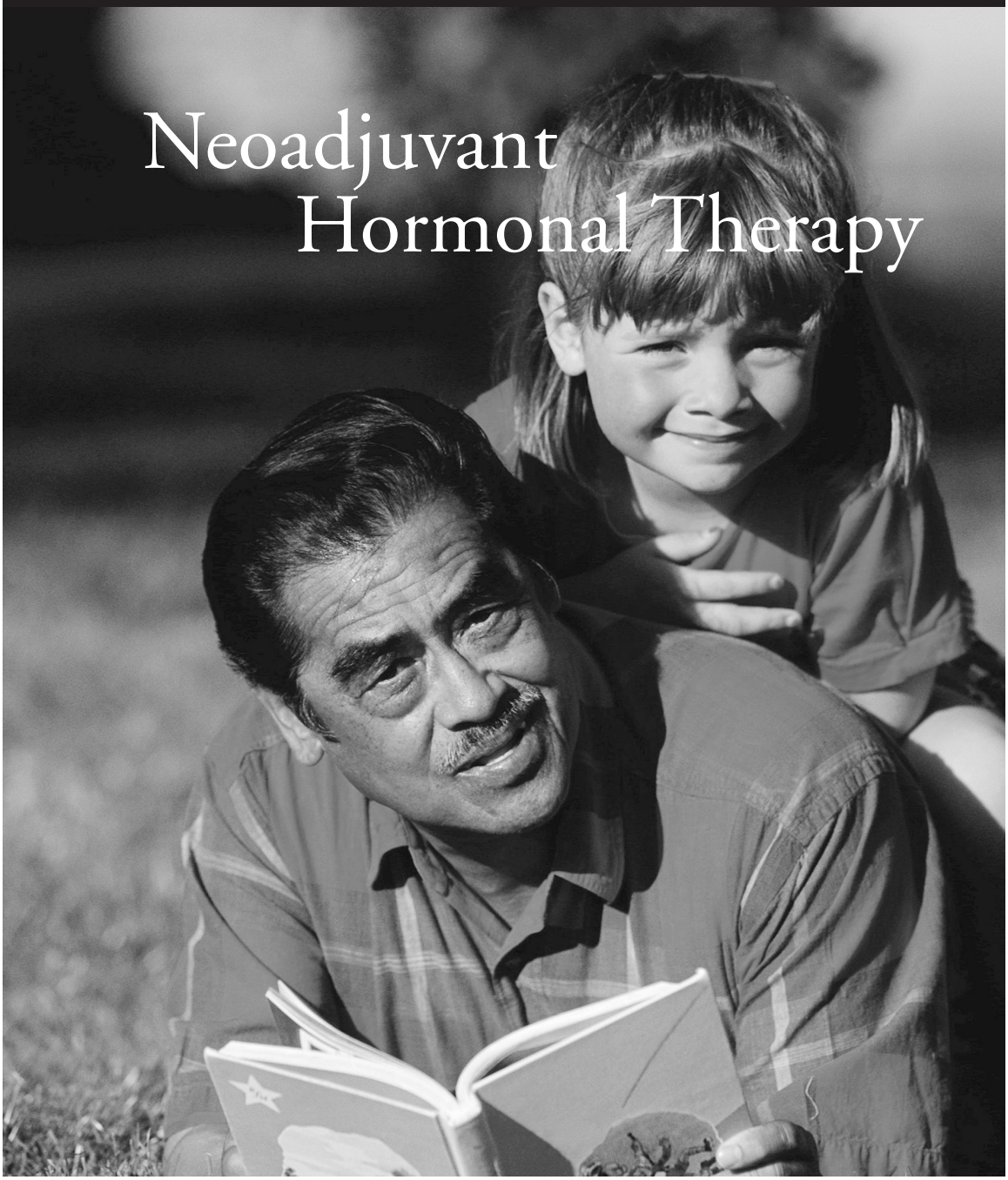
At this time, the favorable results of cryotherapy are not well-established. There are no long-term studies on cryotherapy so it is unknown whether it cures prostate cancer (studies would have to track patients 15 years after the procedure to know this). Doctors are constantly improving the technology, so the studies that have been done describe a procedure that is no longer performed (for example, doctors now use argon gas to freeze the prostate instead of liquid nitrogen; the number of probes used can vary from four to 30). Cryotherapy is also not performed at all hospitals, so you will have to check whether it is available in your area. Unless it is performed as part of a clinical study, one has to be cautious about choosing cryotherapy to treat prostate cancer. (See Chapter 14 on clinical studies.)

What are the side effects or disadvantages of cryotherapy?

As with surgery and radiotherapy, the main side effects are incontinence (4 to 27% in various studies) and impotence (about 40% to 90% of patients, in different studies measuring different time frames). This is because structures, such as the urethra and erection nerve bundles, are located so close to the prostate and can be harmed by the freezing. Since we have no long term results on cryotherapy, we cannot say whether it is more or less likely to have these side effects than surgery or radiation. Erectile function can improve over time and patients may be able to use aids such as Viagra to achieve erections. Cryotherapy is not always effective the first time it is done, and so the procedure may have to be repeated (this is both an advantage and a disadvantage). Physician experience with this technique varies widely.

Chapter 7

Neoadjuvant Hormonal Therapy



Enhancing Standard Therapies

Neoadjuvant hormonal therapy is sometimes used to enhance the effectiveness of standard therapies (surgery or radiation). It is not used alone as its own therapy.

The term "neoadjuvant hormonal therapy" needs some description. Loosely translated, "neoadjuvant" refers to an adjuvant therapy (therapy in addition to primary treatment), given before ("neo") the primary treatment. "Hormonal therapy" implies treatment with hormones. (We'll discuss the role of hormones later in this chapter.) In other words, neoadjuvant hormonal therapy is hormonal therapy that is given in addition to primary treatment (surgery or radiation) but before the primary treatment.

Why do hormones play a role?

Recall that the prostate gland is an accessory sexual organ in men. It is helpful for sexual function, but is not essential for life. The prostate's survival and adequate functioning depends on male sex hormones, such as testosterone. If deprived of male sex hormones, healthy prostate cells go into hibernation. They don't die, but they become vegetative or dormant. Prostate cancer cells respond the same way. Without male sex hormones, the cancer cells become dormant, which delays the cancer's progression. (However, cancer cells do recover after a few years of male hormone deprivation. While you are taking hormones, though your prostate cancer is suppressed, it is still there. For men with advanced cancer, hormone therapy gives them a chance to feel better and live longer. However, if a man stops taking hormones, the cancer starts growing again.)

In hormonal therapy for prostate cancer, hormone production is suppressed, usually with medications. Taken in pill form, by shot, or combined pill and shot, these drugs suppress the testes and adrenal glands, therefore decreasing the level of male sex hormones circulating in the blood.

"Anti-androgen" drugs are commonly used in hormone therapy because they counter the typically male effects of male hormones. Normally, the male hormones have to travel via the blood to reach prostate cells (cancerous and non-cancerous cells) and become attached to the surface of these cells. Then they slowly wriggle into the cells to start their actions. The male hormones have a limited number of spots ("androgen receptors") available on the surface of the cells where they can attach. The anti-androgen drugs have a chemical structure similar to that of male hormones; therefore, the anti-androgens compete for these few androgen receptor locations and block real male hormones from getting into the prostate (cancer) cells. These anti-androgens are also called "hormones."

Are there other types of hormones used in therapy?

- Another hormone, called "LHRH agonists," is sometimes used in hormonal therapy. LHRH agonists depress the function of the pituitary gland, a pea-sized gland located in the middle of the brain. Normally, the pituitary secretes an "LH" hormone, which then signals the testes to secrete testosterone. LHRH agonists cause the pituitary to lessen its signal to the testes, so testosterone secretion by the testes declines.
- The adrenal glands, located just above each kidney, also secrete some weak male hormones. Giving LHRH agonists and anti-androgens together reduces the action of all androgens (testosterone and weaker hormones like those from the adrenals). This combination of drugs is sometimes called total androgen blockage (TAB) or total androgen deprivation (TAD).

An older form of hormonal therapy involved taking female hormones such as estrogen to counteract the effects of male hormones. This approach was common for several decades but is rarely used today.

Are there any other ways to block the production of male sex hormones, in order to slow the growth of prostate cancer?

Surgical removal of the testes ("orchiectomy") also will halt the production of testosterone, the major male hormone. Although a minor surgical procedure, testes removal is usually not necessary for men with early-stage prostate cancer. However, orchiectomy may be recommended for patients with metastatic prostate cancer, just as hormonal therapy alone might be suggested when cancer has spread outside the prostate.

What about the neoadjuvant aspect of hormonal therapy?

Recall that neoadjuvant hormonal therapy means: hormonal therapy given in addition to a primary treatment, before the primary treatment. The primary treatment for prostate cancer is radiation therapy or surgery.

Why is neoadjuvant hormone therapy (NAHT) used?

NAHT (pronounced "naught") can significantly reduce the number of cancer cells in the body before the primary treatment. Thus, NAHT may make surgery or radiation therapy for some early-stage cancers more effective.

What is the rationale of using NAHT before radical prostatectomy?

Until recently, hormonal therapy in prostate cancer was considered "cytostatic" in medical lingo; that is, it kept the cancer cells ("cyto") static (stagnant). The cancer cells neither died nor grew.

Recent scientific evidence suggests that hormonal therapy may, in fact, push some cells into a path of suicidal death called "apoptosis." Some of the prostate cancer cells will die when deprived of male hormones. In addition, the prostate gland shrinks in size with hormonal therapy.

These two processes—death of some of the cancer cells and shrinking of the prostate—are believed to achieve three things at the time of radical prostatectomy:
1. Make the operation easier.
2. Make it easier to obtain clean margins by removing all of the cancer.
3. Control PSA levels after surgery.

However, so far, no studies show that long-term survival is improved with NAHT before radical prostatectomy. So it is generally not recommended before prostatectomy.

What is the rationale of using NAHT before radiation therapy?

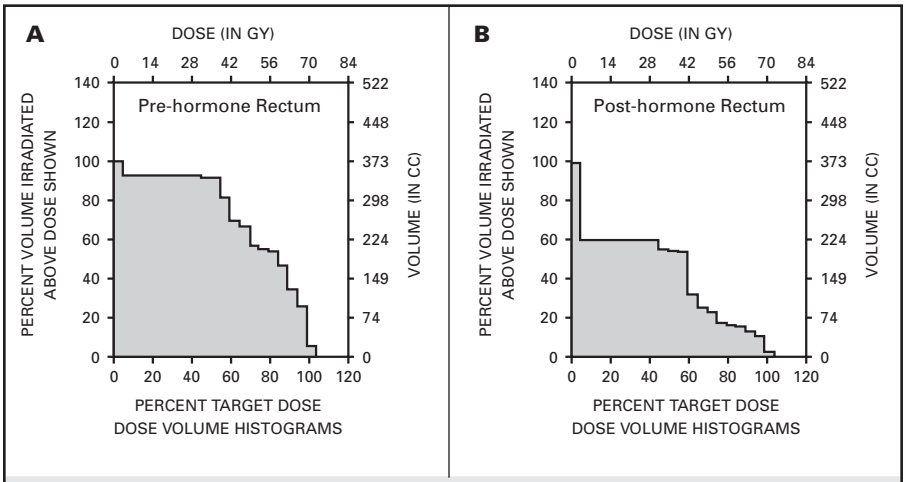
As with surgical treatment, radiation therapy is believed to be more effective after some of the cancer cells die through the process of apoptosis.

The success of radiation therapy depends on the number of cancer cells that the radiation has to tackle. The smaller the number of cancer cells, the better is the chance of cure. Thus, by killing a certain fraction of cancer cells before the primary treatment, hormonal therapy can enhance the chances of cure with radiation therapy.

There is a second reason why NAHT can be beneficial before radiation therapy. Hormone therapy causes the prostate gland to shrink; after two months of hormonal therapy, a 30-40% reduction in prostate size can be expected. Therefore, the amount of bladder and rectum in the path of the radiation will be reduced because a smaller radiation field size will be needed to reach this smaller prostate [see Figure 19]. Note that decreasing the tumor size is not the same as down-staging the cancer; we do not know for sure if this ever occurs.

There may be a third advantage of NAHT/adjuvant hormone therapy with radiation therapy, but this is still theoretical. The changes in cell cycle events induced by hormones may help x-rays to kill more cancer cells. Hormones may make cancer cells more sensitive to the killing effects of radiation. Two major American studies (RTOG 8631 and RTOG 9413) and one major European study (EORTC) suggest that NAHT is helpful before radiation therapy in terms of improved cancer control. At least three American studies also show that the volumes of rectum or bladder in the path of radiation are reduced with NAHT (see Related Articles, Resources chapter at the end of this book).

Figure 19



On the left (A), the shaded area of the rectum represents the volume of the rectum receiving radiation doses if radiation therapy was given without hormones; on the right (B), for the same patient, the amount of the rectum being irradiated is shown after hormone treatment, with shrinkage of the prostate gland. Note how much smaller the shaded area is in the right figure versus the left figure. This represents a benefit because less of the rectum receives radiation doses. Similar advantages occur for the bladder.

Can hormone therapy be used before brachytherapy?

Hormones can be used before brachytherapy to reduce the size of the prostate, which can make it easier to place the seeds in the best places.

What are the side effects of neoadjuvant hormonal therapy?

The side effects of NAHT can be a nuisance, but usually are not serious. These symptoms usually disappear a few months after hormonal therapy ends. The goal of hormonal therapy is to provide the greatest androgen blockade with the least side effects.

Common side effects include:

- Hot flashes (sudden feelings of being very warm).
- Loss of sexual desire or decreased sexual performance.
- Diarrhea.
- Decrease in energy level.
- Swelling of the breasts (gynecomastia), sometimes with pain. Radiation treatment at low doses can prevent this.
- Weight gain.
- Impotence.
- Reduction in muscle and bone mass, leaving you more prone to broken bones (osteoporosis), when used long term.
- Nausea (in some cases).
- Liver damage in rare cases.
- Tumor flare – pain at tumor sites in the first few weeks, due to a temporary increase in testosterone levels.

Does hormonal therapy affect PSA level?

Generally, the PSA level declines with NAHT. Often, the decline in PSA is dramatic.

How long is NAHT given?

In most studies and clinical practices, NAHT is administered for two to six months. There is some evidence that longer treatment is more effective at destroying the cancer. However, it has not been well-documented whether sexual function and other symptoms will return to normal with a longer NAHT duration, as they do with the shorter duration of NAHT.

(In my practice, if the prostate gland becomes significantly smaller and the PSA decline is remarkable, I begin radiation therapy after two months of NAHT and continue hormonal treatment for two months during the radiation therapy.)

Why continue NAHT during radiation therapy?

There are two reasons. First, studies show a benefit when NAHT is administered during radiation therapy, in addition to being given prior to radiation. Also, if hormone therapy is stopped before radiation therapy begins, the prostate might return to its original size during the radiation therapy. This would compromise the effectiveness of radiation therapy because the prostate gland might expand outside of the radiation fields, which were designed while the prostate was shrunken from hormone therapy. Thus, the cancer would not be fully irradiated.

Because of these two reasons, it is advisable to continue hormone therapy during the period of radiation therapy.

Can hormones be used after radiation or surgery?

This is known as adjuvant hormonal therapy, and it may get rid of any cancer cells left behind after surgery or radiation. Hormonal therapy will attack any cancer cells that have spread elsewhere in the body, as it is a systemic therapy.

Hormonal Resistance

We noted earlier that the prostate gland and prostate cancer are hormonally controlled. That is, male hormones are necessary for the normal function of the prostate gland and for the activity of prostate cancer cells.

When deprived of male hormones, the prostate gland and prostate cancer cells go into hibernation: the size of the prostate gland decreases and the prostate cancer cells become inactive. The prostate cells secrete less PSA or no PSA at all; the PSA can even reach zero if the male hormonal influence is removed.

Depriving normal and cancerous prostate cells of male hormones can induce "Apoptosis" or suicidal cell death. Scientists and physicians do not yet know what percentage of cells commit this apoptotic suicide.

However, the surviving normal cells—and, especially, the cancer cells—do not remain dormant forever when deprived of exposure to male hormones. After a period of time the cells recover, rebound, and start reproducing again. This is known as hormonal resistance. Hormonal resistance usually begins about one to three years after hormone deprivation originally occurred.

Does the term "hormonal resistance" accurately describe this phenomenon?

Not really, but it's the term commonly used in the medical world. A more accurate description would be "resistance to hormone deprivation" or "hormone deprivation resistance" because the cells actually become resistant to the state of being hormone-deprived.

Are there ways to delay hormonal resistance?

Some doctors prescribe "intermittent hormonal therapy," which consists of having a patient take hormones, then take a break from them, then go back on hormones, and so on. (This is also called "intermittent androgen blockade.") They believe that when patients use hormones without a break, the cancer is given the best chance to adapt to hormones. The interruptions in hormones disrupt the cancer from adjusting to the testosterone decline, or at the very least make it take longer for the cancer to adapt to hormone therapy. Generally, doctors monitor a patient's PSA to determine when to go on and off hormones – when PSA drops to a certain level and stays level, the patient goes off of hormones. When PSA rises again, the patient goes back on hormones. This is still an investigational therapy.

If prostate cells need male hormones to function, what happens when hormonal resistance occurs?

After being deprived of male hormones and lying dormant for several years, prostate cells and prostate cancer cells eventually adjust and learn how to grow without the male hormone. These now hormone-resistant cells begin to multiply, and the cancer starts to grow.

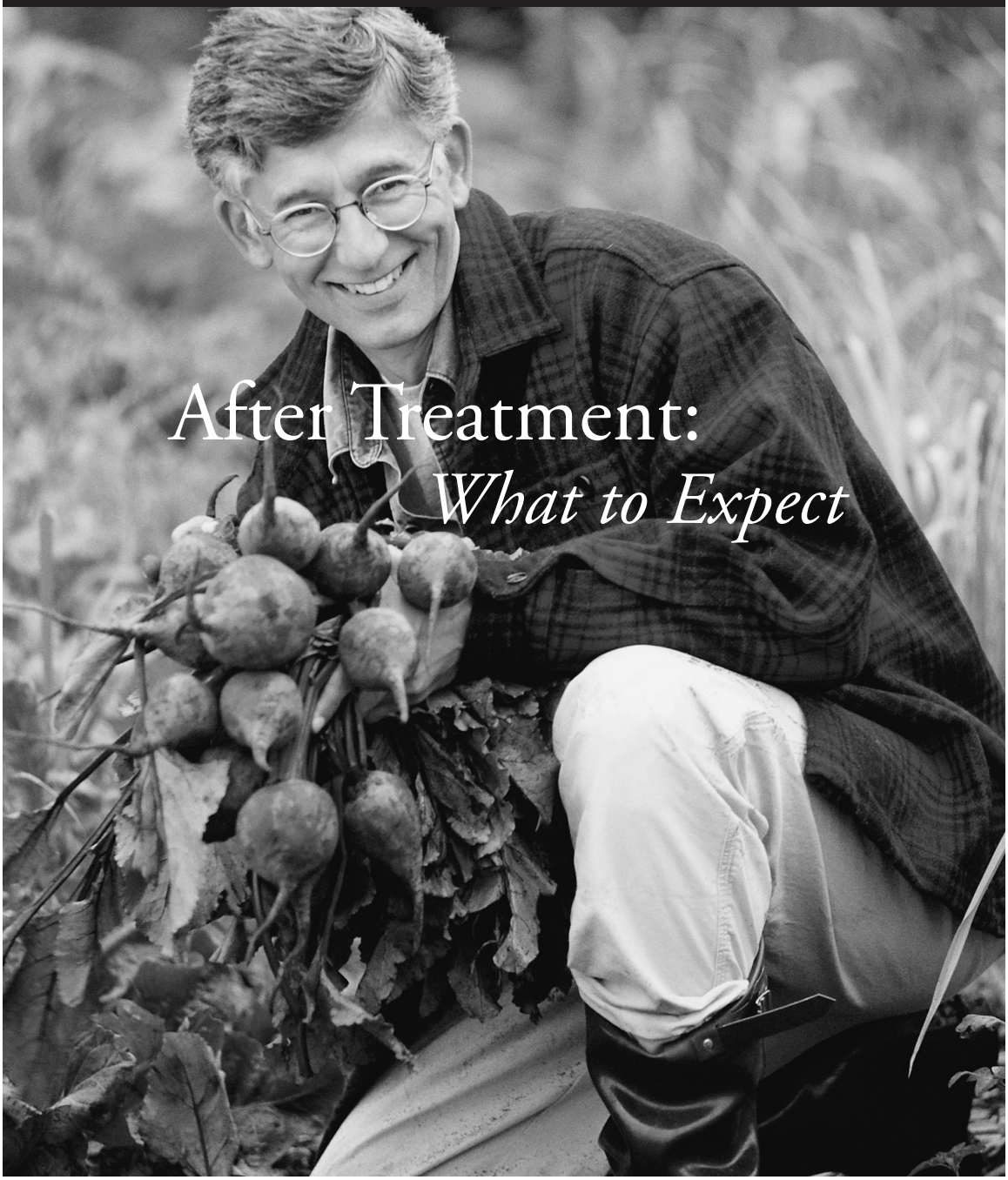
It is hypothesized that a fraction of prostate cancer cells are actually born with hormonal resistance, that is, the ability to live and multiply without male hormones. Through many generations of selective reproduction, these hormone-resistant cells ultimately become the predominant population of cancer cells (an example of survival of the fittest) and spread to other body tissues.

Until now, there have been very few solutions to this problem of hormonal resistance, which often happens in patients with metastatic prostate cancer after many years of hormonal therapy. This phenomenon often contributes to the final cancer stage and death of these patients.

What are some of the options for the man with metastatic cancer who is now hormone resistant?

- Total androgen blockage. If the patient received therapy with a single hormone ("monotherapy"), then combined hormonal therapies may be initiated. For example, the patient may receive an anti-androgen (such as Flutamide or Casodex) plus an LHRH agonist (such as Lupron or Zoladex).
- Flutamide withdrawal or hormone withdrawal. For some patients who develop resistance while receiving hormones, stopping the hormones actually causes the cancer to stop growing. This is generally known as "antiandrogen withdrawal."
- Other anti-androgens. Sometimes, switching from one anti-androgen drug to another is helpful for overcoming hormone resistance. The androgen receptors seem to distinguish between the slightly different chemical structures of different drugs.
- Chemotherapy drugs. The U.S. Food & Drug Administration (FDA) has approved two chemotherapy drugs for treating prostate cancer in hormone-resistant patients, Mitoxantrone and Taxotere. Both are given in combination with prednisone, a steroid. Mitoxantrone was the first chemotherapy drug that the FDA approved for use in prostate cancer treatment; it lessens bone pain in some patients but does not improve survival. In May 2004, the FDA also approved Taxotere (docetaxel) injection in combination with prednisone after a clinical trial found it helped some patients live longer.
- Investigational therapies. When no other treatments seem effective, some patients choose to try investigational therapies, as part of monitored clinical trials or studies. Clinical studies evaluate the effectiveness and risks of potential new therapies. Clinical studies give patients access to the very newest treatments before the FDA has approved them for general use. (For more on clinical trials, see Chapter 14.)
- Palliative treatments to relieve cancer symptoms.

Chapter 8



After Treatment: *What to Expect*

While no two men have the exact same experience after treatment for prostate cancer, there are some common reactions that can be expected. The recovery experience and issues after radical prostatectomy are different than after radiation therapy.

Recovery After Radical Prostatectomy

What can I expect immediately after the surgery?

In the hospital immediately after surgery, a Foley catheter will be placed in your penis and it will stay there for up to three weeks. Your surgeon will also have created two small drains in your lower abdomen, to let any loose blood or urine out; these will remain for up to four days. You will have a patient-administered analgesic pump (PCA) to allow you to manage your pain medications. Do not be shy about asking for more medication if you are in pain, as doctors tend to be conservative about prescribing pain medications – only you know how much pain you are in. Within a day you should be able to take short walks within the hospital. By the time you return home, you will have improved greatly.

Although each man recovers at his own pace, you can expect to go home from the hospital within about three to seven days after the surgery (assuming there are no complications). Your first goal will be to regain your strength and functions after surgery. (See the "Resources" chapter at the end of this book to find some books by men, such as M. Korda, describing their recovery from radical prostatectomy.)

Do:

- Follow the exercises recommended to regain urinary control. These exercises are very important and helpful.
- Try to be as active as possible, without straining yourself. Activity helps build your body's strength during this recovery period. Exercise as directed by your surgeon.
- Return to sexual activity after your recovery period, if you want to and are capable. If you feel uncomfortable or uneasy about sexual intimacy after surgery, discuss it with your physician. Note that you will now be sterile (because the connection between the testes and the penis are disconnected and your ejaculations will be dry), so birth control techniques will be unnecessary.
- Keep your follow-up appointments with your surgeon.

What can you expect at the follow-up appointment?

You will meet with your surgeon about two or three weeks after the surgery. During this time, the surgeon will probably conduct a thorough physical examination and check your PSA level to assure that it is declining at the proper pace. (See information at the end of Chapter 2 about PSA half-lives.) Depending on your recovery rate and health status, the surgeon may perform additional tests.

What should you ask the surgeon?

This is an excellent time to ask the surgeon about the status of your cancer and your expected recovery. You may want to ask:

- What did the pathology tests show? (i.e., how large was the tumor, what was the Gleason Score, were the seminal vesicles or capsule invaded with cancer?)
- What exercises should I perform?
- What is my current PSA value, and how does that compare with my PSA before surgery?
- If my physician tells me the surgery was inadequate (did not remove all of the cancer), what are the next steps to consider? (See Chapter 9.)
- Were one or both nerves spared? (Ask this if you had nerve-sparing prostatectomy.)

What role does the pathologist play, and how does that influence the patient after surgery?

Like unseen angels, pathologists work behind the scenes so their contributions often go unrecognized. It is very important to have an experienced and expert pathologist on your cancer care team, as the pathologist's findings will help guide decisions about your treatment. Pathologists determine:

- Was it truly cancer? (Very rarely, the biopsy might have been interpreted as cancer, but none may be found at the time of surgery. Why? There are several possible explanations: All cancer might have been removed by biopsy; there might have been a misdiagnosis; or hormonal treatments might have eliminated some cancer cells.)
- What was the size of the tumor?
- What was the Gleason Score? The Gleason Score is more reliable after surgery than after the biopsy.
- Was there more than one tumor? If so, how many?
- Was the cancer confined to the right half or left half of the prostate, or did it involve both halves?

- Was the capsule (the outer covering or the wrap) of the prostate gland invaded by the cancer? (It is better if the capsule is not involved.)
- If the capsule was invaded by cancer, was it in a single spot, or spread around?
- Were the seminal vesicles invaded by cancer? (It is better if they are not invaded.)
- Was the apical margin clean?

Removing the apical part of the prostate gland is the most difficult surgical aspect of radical prostatectomy. The prostate's tip ("apex") is close to the top of the penis and the urethra within the penis. Continuity is necessary between the bladder and penile urethra to provide normal urinary function. This presents a challenge to the surgeon. If too much of the sphincter is removed at this point, incontinence will occur. If too little of the sphincter is removed, some cancer cells may be left behind. Most relapses after radical prostatectomy occur at this spot. You may ask for a copy of the pathology report. You can skip most of the technical details and look for the pathologist's comments (probably near the end of the report) where the pathologist usually summarizes the overall findings, often in simple terms.

◆ Advanced Notes

About the pathology tests: As described in Chapter 5, the prostate gland and other tissues removed during surgery are sent to the pathologist. Once removed from the body, it is important to distinguish the front, back, left and right sides of the specimen. Some surgeons mark the right and left sides of the prostate gland with different colored ink so that the pathologist can distinguish the right from the left and properly orient the specimen for analysis. Other surgeons stitch different labels at the top and bottom of the specimen to aid the pathologist.

Recovery After Radiation Therapy

Do:

- **Exercise in moderation.** Activity keeps your body strong.
- **Drink plenty of fluids**, preferably water and fruit juices. (Avoid too much caffeine, soda pop or alcohol.)
- **If your stools are hard, take a stool softener** such as Metamucil. This helps to prevent bleeding from hard stools. Also, be sure to get plenty of fiber in your diet. High fiber cereals, whole grain breads, and fresh fruits and vegetables can help.
- **If you have sexual desire and intact sexual function**, there is no need to avoid intimate relations. Sexual activity does not stimulate the prostate cancer to grow.
- **If you have sexual desire but get no erection**, ask your doctor for help. There are many aids available today to assist erection, such as oral medications (Viagra® and others), vacuum pumps, safe intrapenile injections, or pellets.
- **Treat yourself** to an occasional alcoholic drink, if you wish. Moderate amounts of alcohol will not affect your treatment or make the cancer grow back. As in most things, however, moderation is advised.
- **For any symptoms** you are experiencing, ask your doctor or nurse for suggestions on how to relieve or cope with them.

Patients are usually asked to return to see the radiation oncologist about two weeks after the last session of radiation therapy. The main purpose of this first visit after the treatment is to see whether the side effects—such as diarrhea or urinary symptoms—have subsided. In more than 90% of patients, these symptoms do subside in two weeks. The doctor will check your skin and ask you to use moisturizing lotions on the dry skin. Blood will be drawn for PSA. A digital rectal examination will be done to feel the prostate gland, if you do not have too much burning in the rectal region.

If you had been on hormones prior to and during radiation therapy, they are usually stopped on the last day of your radiation therapy. If not, they probably will be stopped on this first follow-up visit. (In some cases, the doctor may decide to continue the hormonal treatments.)

If you ask the radiation oncologist, "How am I doing? Is the cancer all gone? Am

I cured?" he or she cannot answer these questions immediately. After radiation therapy, the cancer's response takes months to manifest. Dead cancer cells have to be gradually disposed of by the body. Some cancer cells, even if technically dead (i.e., they cannot multiply), may continue to "eat and breathe" for some time.

Then, when can a person tell the effectiveness of radiation?

Results may start to show three to six months after radiation therapy ends; and should definitely be evident one year after therapy. By then, there should be improvement witnessed by digital rectal examination and a decline in the PSA level.

However, digital rectal exam is not a very accurate way to assess the effectiveness of radiation therapy. Positive evaluation is difficult to make because the physician may also feel scar formation after the radiation therapy, plus benign prostate disease (which is not altered by the radiation). PSA is a better measure of the effectiveness of radiation therapy.

What should the PSA level be after radiation therapy?

Unlike surgery, radiation leaves the prostate gland intact. Not all normal cells are killed. Therefore, the PSA level will not go to zero after radiation, as it may do after surgery.

Then how does a person know whether radiation therapy was successful?

There should be a steady decline in PSA. By 12-18 months after therapy, PSA level should be as low as possible and preferably less than 1 ng/ml. (Please refer to the discussion of "PSA nadir"in Chapter 5).

Will there be another biopsy after radiation therapy?

A routine biopsy to document whether all the cancer is eradicated is not necessary, unless you sign up as part of a clinical study. However, biopsy is safe and usually not uncomfortable after RT. Therefore, your physician may recommend a follow-up biopsy if your PSA is rising, if he feels any suspicious areas during the digital rectal exam, or if he plans additional treatment.

What should you ask the radiation oncologist during follow-up?

During your follow-up visit with the radiation oncologist, you may want to ask:

- Did the digital rectal exam suggest any suspicious findings?
- What is my PSA value, and how does that compare with the pre-therapy value?
- Is my PSA level declining?

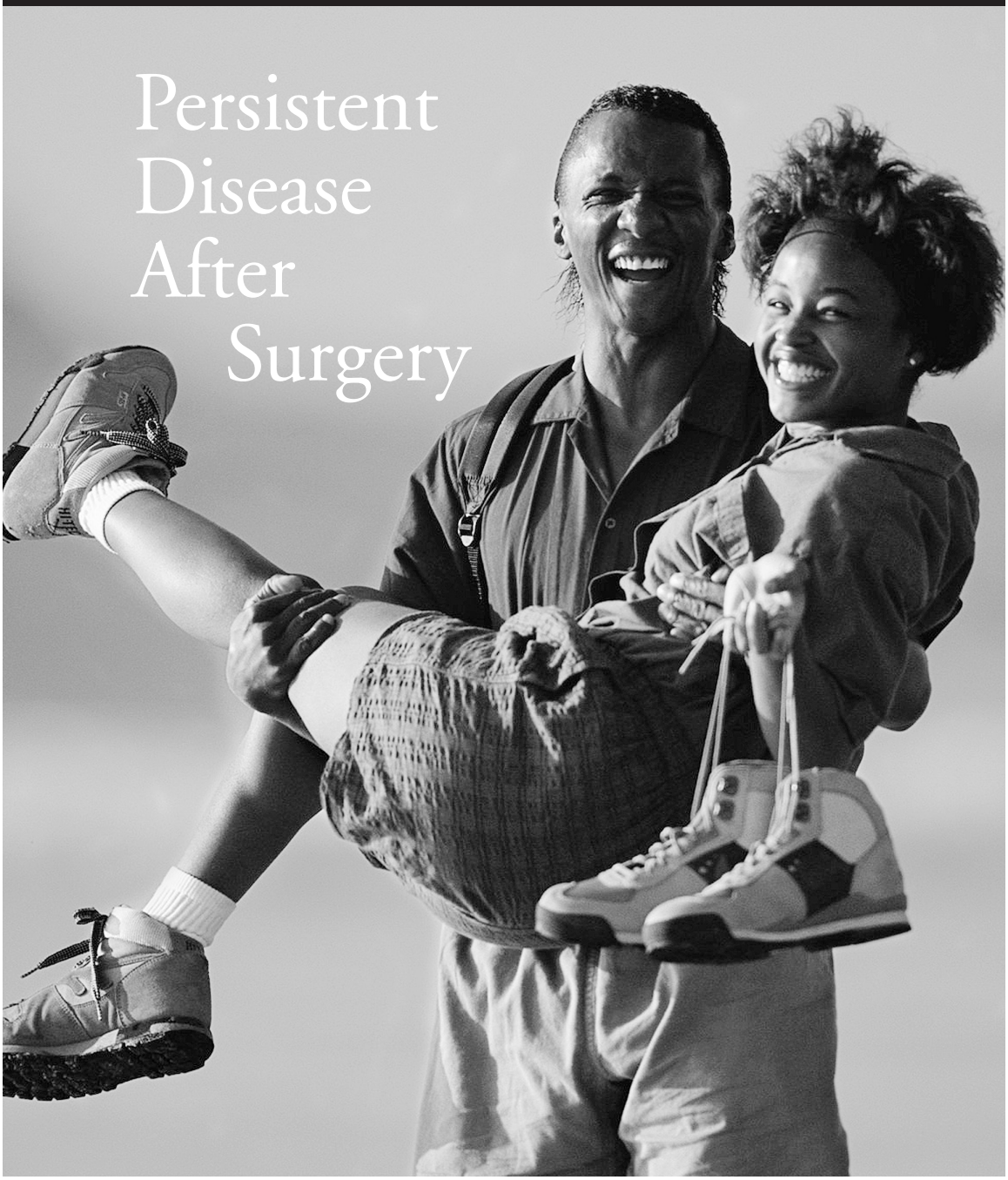
Do not panic if PSA values have actually gone up by the time of your first visit. That often happens. However, it should start to decline within two or three months. You will have to continue to have follow-up visits with your radiation oncologist every three or four months to monitor the status of your cancer.

What is the worst that can happen after radiation therapy?

The worst side effects could be rectal ulcer, bladder bleeding and colostomy. Fortunately, these complications are very rare. (Chances are 1 in 500 to 1 in 1,000.)

Chapter 9

Persistent Disease After Surgery



"Persistent disease after surgery" implies that some cancer cells remain after radical prostatectomy.

How do I know if I have persistent disease after surgery (meaning that some cancer still remains)?

The following factors may indicate that some prostate cancer cells remain. (However, these signs do not necessarily mean that there is more cancer.)

- The capsule of the prostate gland was invaded by cancer.
- The margins of the removed prostate were positive.
- The seminal vesicles had some cancer.
- The apex was positive.
- After surgery, PSA value never reaches zero or less than 0.2-0.5 ng/ml.
- After surgery, PSA does reach zero, but starts to increase again.
- The physician's digital rectal examination suggests a cancer recurrence in the prostate area and a follow-up biopsy is positive.

What are the options if cancer recurs or was never completely eliminated?

This is a very controversial subject. Previous experience shows that additional radiation therapy prevents cancer from growing back in the prostate area if the radiation is given within three to six months after surgery, under the following circumstances:

- Positive margins.
- Capsule is involved.
- Seminal vesicles are invaded.

Whether a patient gains more years of life with this approach is not well documented. Randomized studies are addressing this issue (see Chapter 14 on Clinical Trials).

What can a patient do at this point?

Consider the following:

- You underwent major surgery to have the cancer eradicated.
- Radiation therapy is an effective agent for killing cancer cells.
- It is easier and more effective to kill a few cancer cells with radiation than when

there is a large tumor (assuming all of the cancer cells are located close to each other and not scattered throughout the body).
- Radiation has its own side effects and potential complications. The side effects of surgery and radiation, when one follows the other, will be worse than they would be for either treatment alone.
- There is no strong evidence that radiation after surgery significantly increases incontinence or impotence rates. (The physician will wait for good healing from the surgery before beginning radiation therapy.)

What should you do if the PSA starts to increase two to three years after the prostatectomy surgery?

The following diagnostic tests should be done to determine whether cancer has recurred:
- Digital rectal exam, to determine whether there is cancer recurrence in the prostate area.
- Ultrasound examination of the prostatic bed.
- Bone scan to identify any cancer spread to the bones.
- A chest x-ray to determine if cancer has spread to the lungs.
- A new test called "ProstaScint" may be considered to identify the location of any cancer recurrence.
- CT scan to evaluate whether large lymph nodes in the abdomen or pelvis have cancer. If normal-size lymph nodes have cancer cells, then CT may not detect it.

After these tests, what are the options?

Clearly, the options depend on the test results.

Scenario I: Cancer recurs in the prostate area only.

Tests results show:
- Recurrence of cancer in the prostate area.
- Bone scan is negative.
- CT is negative.
- Chest X-ray is negative.

If cancer recurs in the prostate area but has not reached the bones, lymph nodes or lungs, the treatment options include:
- Radiation therapy. The patients most likely to benefit from radiation therapy after prostatectomy are those in this group, where cancer recurs in the prostate area only.

- Hormonal therapy—this may make radiation treatment after prostatectomy more effective.
- Watchful waiting.

Scenario II: Bone scan and X-rays of bones are positive, indicating spread of cancer.

If cancer has spread to the bones, treatment options are no longer given with the intent to cure, and include:

- Hormonal therapy.
- Radiation therapy.
- Strontium therapy (see Chapter 10).
- Samarium therapy.
- A combination of the above.
- Other new investigational treatments.

Scenario III: Lymph nodes are involved with cancer, but everything else is negative (free of cancer).

In this scenario, you may consider the following treatment options:

- Radiation therapy.
- Hormonal therapy.
- Radiation therapy plus hormonal therapy.
- Watchful waiting.
- New investigational therapies.

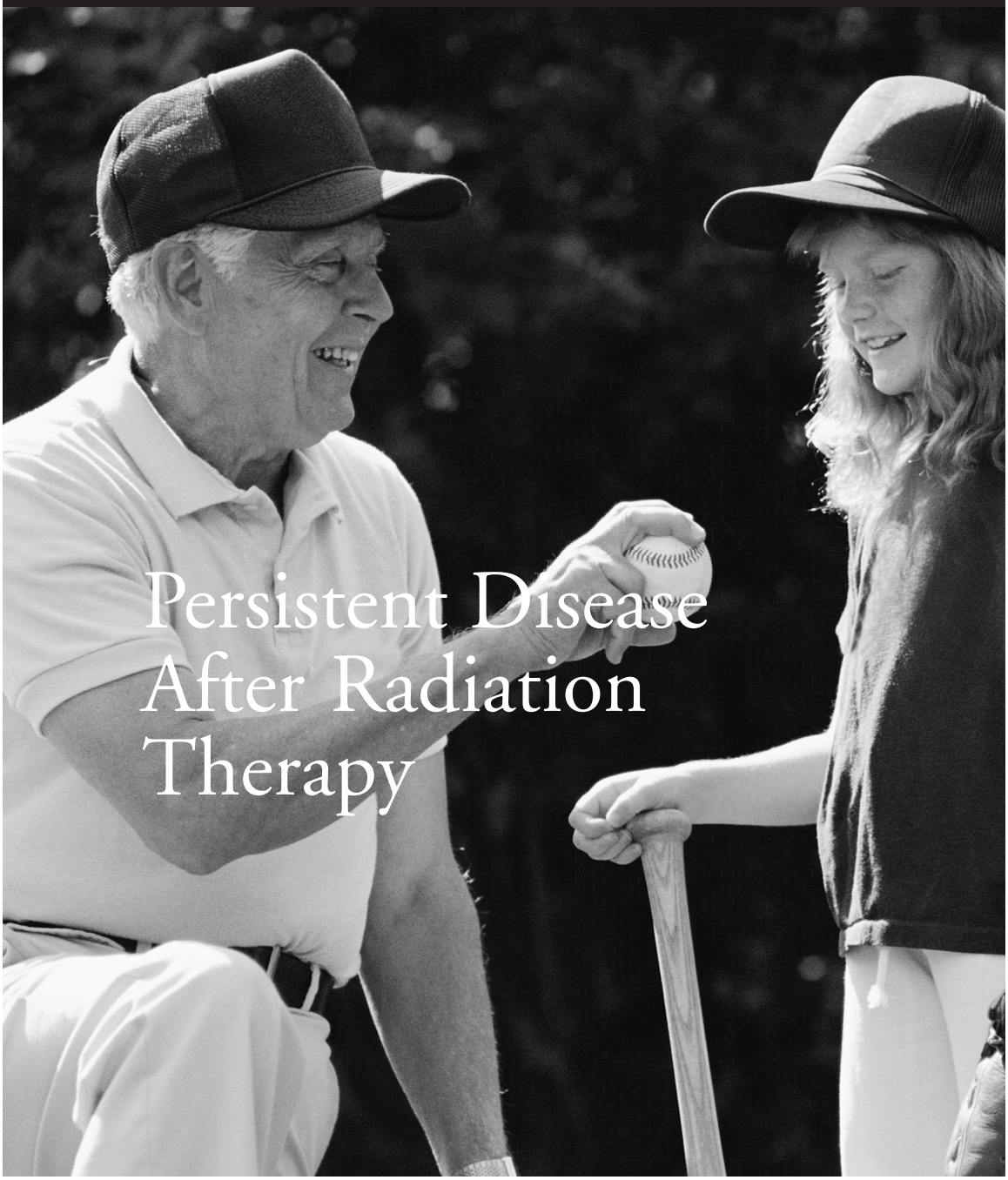
Scenario IV: All tests are negative, but PSA is rising.

If your PSA level is rising but other tests show no signs of cancer, this suggests that there is cancer somewhere in the body, but tests cannot pinpoint the location. You may want to consider these treatment options:

- Hormonal therapy.
- Watchful waiting.
- Investigational therapies.
- Radiation therapy.

There are new hormonal combinations which may allow the patient to retain sexual function. For example, a combination of Flutamide® and Proscar® or similar combinations have been tested. At this time, these combinations are investigational and are being used only within medical research environments.

Chapter 10



Persistent Disease After Radiation Therapy

"Persistent disease after radiation therapy" means that radiation did not destroy all of the cancer cells.

How does one know that there has been persistent disease after radiation therapy, especially considering that it can take up to a year to show full results?

The following factors may indicate that radiation therapy did not destroy all of the cancer, or that cancer has recurred.

- PSA levels never declined to less than 4 ng/ml.
- PSA levels declined, but then start to increase. The American Society for Therapeutic Radiology and Oncology (ASTRO) guidelines define radiation therapy failure as three consecutive rises in PSA after it reaches its nadir (lowest point). ASTRO recommends that patients have a PSA test every 3-4 months for the first two years after radiation therapy, and then every six months after that, so it may take more than a year to declare that there has been persistent disease after radiation therapy. As mentioned in Chapter 6, I have another, more complicated but more accurate definition of treatment failure. Waiting for three rising PSA values may be too stringent when two large consecutive rises clearly indicate treatment failure or when the interval between determinations is long. My nadir definition correlates more closely with clinical outcomes than the standard ASTRO definition (see Jani et al in the references). Other definitions of treatment failure are currently being developed (ASTRO consensus panel).
- Digital rectal exam suggests:
  1) that cancer was never completely eliminated, or
  2) recurrence of cancer that had previously disappeared.
- Biopsy of prostate shows cancer after PSA levels suggested possible relapse.
- Bone scan is positive now (but was negative before radiation began).
- CT scans show large lymph nodes.
- Other tests or biopsies show recurrence of cancer.

What are the treatment options after inadequate radiation therapy?

Treatment options vary, depending on each patient's condition. Unfortunately, patients cannot be retreated with external radiation.

Scenario I: PSA rising, but no signs that cancer has spread to other organs.
Test results:
- Increasing PSA levels.
- Digital rectal exam, bone scan, chest X-ray and CT scan are all negative.
- Patient has decided not to have a biopsy of the prostate.

Treatment options to consider:
- Hormonal therapy.
- Watchful waiting.
- Participation in a clinical study of a new treatment.

Scenario II: Cancer recurs in the prostate, but has not spread.
Test results show:
- Positive biopsy in the prostate.
- All other tests are negative.

Treatment options to consider:
- Salvage prostatectomy (surgery).
- Cryotherapy.
- Hormone therapy.
- Watchful waiting.
- Investigational therapies, offered through a clinical trial.

Scenario III: Cancer has spread to the bones, lymph nodes and on lungs.
Tests results show:
- PSA level rising.
- Positive bone scan.
- Positive chest X-ray.

Treatment options include:
- Hormone therapy.
- Radiation therapy.
- Strontium therapy.
- Samarium therapy
- Investigational therapies, offered through a clinical trial.

What is Salvage Prostatectomy?

Salvage prostatectomy is a method of prostatectomy performed after radiation therapy in order to "salvage" or cure a patient whose cancer has not been destroyed by radiation alone. Salvage prostatectomy carries significant risks, with high incontinence and impotence rates and rectal injuries. All things considered, it is not a very successful treatment. More commonly, a failed radiation treatment will be followed by hormone therapy and perhaps a bilateral orchiectomy.

What is Strontium/ Samarium Therapy?

Strontium therapy is a form of radiation that involves injecting strontium into the blood. There are also newer agents that may have some advantages (for example, Samarium). Strontium is a radioactive substance that seeks the bones and may give patients dramatic pain relief. Thus, cancer cells in the bones are then killed. However, strontium is used to control bone pain, and not to cure cancer, in patients with metastatic prostate cancer that no longer responds to hormonal therapy. Strontium can also be combined with external beam radiation.

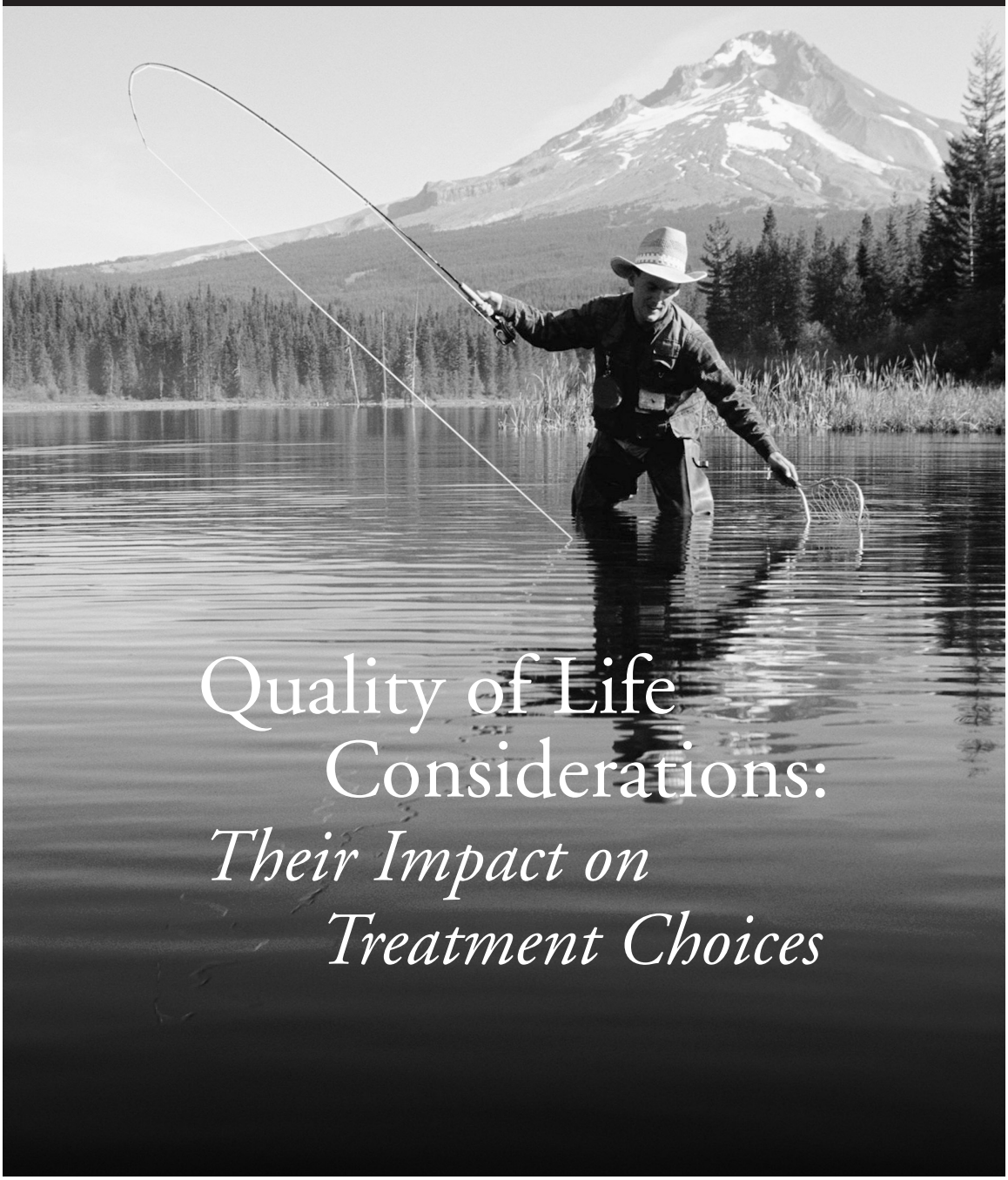
With so many treatment options to consider, how can you decide which is best for you?

Before making a decision about further treatment, try to gather as much information as possible, then discuss the pros and cons of each option with your team of physicians as well as family members or others close to you. There are many factors to consider, such as:

- Your age.
- Your overall health.
- Any other medical problems you may have.
- Any pain or other symptoms you may have.
- Your concerns about potential complications of treatment.
- The expertise and experience of your physician team.
- Your potential comfort or anxiety if no treatment is pursued (i.e., the watchful waiting approach). (See Chapter 5 for more on watchful waiting.)
- Your own personal preferences, and your family's opinions.

Consider all of these factors, ask questions, discuss them with your doctors and family, and then decide. If you are uncomfortable with making a decision, don't hesitate to seek a second or even third opinion.

Chapter 11



Quality of Life Considerations: *Their Impact on Treatment Choices*

When trying to select the most appropriate treatment for prostate cancer, it's important to consider issues that affect your quality of life, as well as the effectiveness and disadvantages of each treatment.

First, consider that prostate cancer grows slowly in many men, making it a chronic disease (a disease that lingers for a long time, such as diabetes or asthma), rather than an acute disease (a disease or illness that strikes hard, often for a shorter duration, such as pneumonia). This chronic aspect is especially true when prostate cancer strikes older men.

In general, prostate cancer is a disease of the elderly. As men age, they also are prone to developing a variety of health problems such as hypertension, heart attacks, strokes, diabetes, benign prostate hyperplasia or arthritis . . . just as they are more likely to develop prostate cancer with advanced age. Each of these diseases causes symptoms, and each carries its own increased risk of death. This complicates the decision-making process for treating prostate cancer because one often must project and compare the outcome of competing morbidities and mortalities. (Mortality means the possibility of death from a disease; morbidity refers to symptoms of a disease or its treatment.) A man must consider whether the disease symptoms and statistical risk of dying from prostate cancer are better or worse than his symptoms and risk of dying from a heart attack, for example.

What role does age play in the decision process?

As men age, the prostate gland often suffers from a condition called benign prostate hyperplasia (BPH). BPH causes urinary symptoms: frequent urination, a burning sensation when urinating, and a feeling of incomplete voiding. These symptoms of BPH are similar to those induced by prostate cancer or cancer treatment (surgery or radiation therapy).

After treatment, it is not easy to decipher whether the symptoms are caused by aging or by the treatment. (Urinary incontinence, however, can be attributed to prostate surgery rather than aging.)

Sexual desire and performance often decline with age, too, which is a natural progression. Both prostate surgery and radiation therapy can cause impotence, although they do not take sexual desire away. (Hormone therapy, however, does diminish sexual desire.) However, thanks to recent improvements in surgical

techniques and radiotherapy methods, the impotence rate with modern treatments may not be significantly worse than that caused naturally by aging.

Also to be considered is the difference between losing sexual desire and losing the ability to have penile erections. Very few remedies exist for loss of sexual desire. However, many innovative approaches are available to assist with erectile function.

What other points should you think about before deciding which treatment course to pursue?

Another point to consider is the anxiety created by a diagnosis of cancer, both for a patient and for his family. For many people, the thought of living with cancer creates stress. This stress can be aggravated if the course pursued is no treatment—watchful waiting.

For example, logic and medical experience may indicate that no treatment is necessary for an 80-year-old man with a Gleason Score 2 cancer. However, emotions may demand an intervention for this 80-year-old man, even if experience shows that, at age 80, he is more likely to die from heart disease than from prostate cancer. If his quality of life will be made worse by the anxiety of not being treated, then it may be best to administer treatment to this individual. Clearly, this is a personal dilemma with no single clear answer for all men.

Can you make an objective decision about quality of life?

Not really. There is no clear black and white distinction; instead, there are many shades of gray when evaluating a person's quality of life.

Quality of life issues are very subjective. They differ significantly from patient to patient, and each has his own perceptions of what is most important to him.

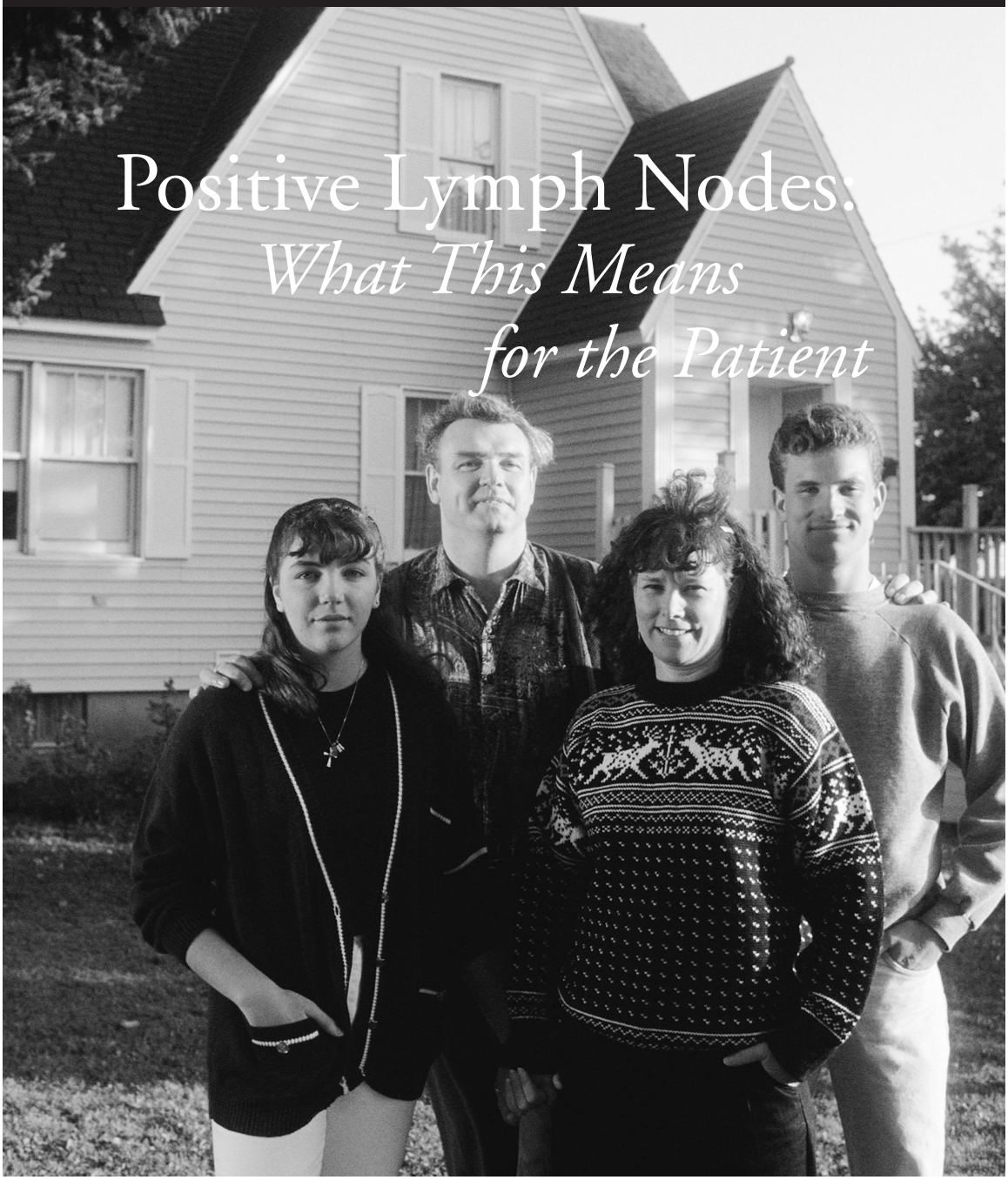
Often, a frank discussion with your physician, followed by a period of reflection, obtaining more information, and talking things over with family and friends, leads to a self-realization on the quality of life tradeoffs between enduring the symptoms of prostate cancer versus enduring the side effects of cancer treatment. This reflection period also allows time to compare the different benefits and symptoms induced by the various treatments, so you can make a clear decision about which approach feels most comfortable to you.

If cancer recurs, do you have to make a decision right away?

No. Fortunately, most men with prostate cancer have a few days or even weeks to make up their mind about the options and their implications, obtain second opinions, and talk to other patients who have similar stages of disease or who have undergone similar treatments. These steps go a long way toward resolving the patient's dilemma.

In rare cases, however, cancer recurrence signals an emergency situation that requires an immediate decision about treatment (see Chapter 4).

Chapter 12



Positive Lymph Nodes: *What This Means for the Patient*

It is not uncommon for a cancer specialist to see patients who had surgery and whose lymph nodes were positive (that is, the cancer had spread to the lymph nodes). This is particularly true at medical centers that provide advanced cancer treatments and conduct cancer research, because these programs attract patients whose cancer has resisted standard therapies.

Why does cancer spread?

In Chapters 1 and 3, we discussed how cancer can spread throughout the body ("metastasize"). Almost all cancers will spread from wherever they begin. This is a biological instinct, like the drive of all species to reproduce. Cancer cells can spread by different means:

1. By local invasion;
2. To lymph nodes and from there into the blood; and
3. Via the blood stream to distant places in the body, including the bones, lungs and liver.

What is the role of lymph nodes?

There are hundreds of lymph nodes throughout the body. When you've been sick with an infection in the past, you may have felt enlarged lymph nodes in the neck (right below your ears and jaw), in your armpits, or in your groin. Lymph capillaries (very small, thin vessels) interconnect all of the lymph nodes. "Lymph" is fluid within the lymphatic system. Lymph fluid travels upward from the feet, and from the head down to the heart.

Lymph nodes act like bodyguards that protect the body from an invasion, such as an invasion of infection or cancer cells. The lymph nodes try to contain the enemy within a confined area in the body. Lymph nodes also work like individualized armies, which assess the type of enemy and try to develop a way to destroy it. When a bacterial infection occurs, for example, the lymph nodes create an antibody to destroy the specific bacteria.

Unfortunately, if the lymph nodes themselves are overwhelmed with a spreading cancer, the lymph nodes can act as a secondary source to spread the cancer further as the lymph fluid travels throughout the body.

To understand the significance of how lymph nodes can spread cancer in men with prostate cancer, let's compare it with breast cancer. There are many similarities between prostate and breast cancer.

- Both breast and prostate cancers arise from accessory sex glands. (In medical lingo, breasts are called "mammary glands"; their main function is to secrete milk for an infant. Any body structure that secretes a fluid is called a gland.)
- Both glands are controlled by hormones. Female hormones control the breast hormones: estrogens and progesterones. Male hormones control the prostate hormones—primarily testosterone—as well as some female hormones.
- The incidence of both breast and prostate cancers is higher in Western countries than in Asian countries, and there has been an increase of both cancers within the past 20-30 years.

So, what can we learn from the breast cancer experience?

From studying the results of breast cancer therapy for women over the years, we can make assumptions that apply to both breast and prostate cancers.

- The smaller the cancer or tumor is, the better the chances are for a cure.
- The smaller the cancer is, the less chance there is that it has spread to the lymph nodes.
- If the lymph nodes are not involved, patients will do better with treatment.
- If lymph nodes are involved, treatment will not be as effective.
- When fewer lymph nodes are invaded with cancer, there is a smaller likelihood that the cancer has spread via the blood to other parts of the body. This means that there is a better chance that local treatment will be effective for long-term survival.

For both breast and prostate cancers, the spread of cancer to lymph nodes and the number of lymph nodes involved provide an indirect measure of how long the cancer has been in the body. The longer cancer has been in the body, the larger the cancer will be, and the more likely it is that cancer already has spread to other parts of the body.

So, if you have positive lymph nodes, what are your options?

When cancer has spread from the prostate to the lymph nodes, you have several treatment options to consider:

- Radiation therapy.
- Hormonal therapy.
- Hormones plus radiation therapy.
- No further treatment.

If a man has advanced cancer with spread to the lymph nodes, how can we suggest "no treatment" as an option?

The "no further treatment" option refers to the watchful waiting approach. (See Chapter 5.) The decision to not pursue further treatment for prostate cancer rests on a man's assessment of his own personal quality of life issues, as discussed in the previous chapter. Each individual must weigh: the ultimate benefits of treatment, the adverse effects of treatment, and the benefits or adverse effects of no treatment.

If a patient is elderly, has many other medical problems, or does not like the complications caused by treatment, one can postpone treatment until symptoms worsen or become bothersome. When deciding whether or not to postpone treatment, the older patient should consider:

- Will the "no treatment" option decrease my life span? Perhaps.
- Will the "no treatment" option improve my quality of life, compared with my potential quality of life after treatment? Perhaps.

The truth is that the medical field does not have enough data to be certain about the outcome of pursuing further treatment for advanced prostate cancer with lymph nodal cancer spread.

Dr. Vijay, what would you do if you were the patient?

If I had positive lymph nodes from prostate cancer, I probably would decide on hormones and radiation therapy: hormones for about two months before radiation and at least two years during and after radiation (the duration of long-term hormone therapy depends on the cancer site and lymph node volume). Then I would stop all treatments and see what happens to my PSA level. If it drops to less than 4 ng/ml, I would then adopt the watchful waiting approach. If my PSA level started to increase again, I would go back on hormones.

Note: This recommendation also assumes that the bone scan, chest X-ray and abdominal CT scan are all negative, with no signs of cancer spread to the bones, lungs or other organs. It also assumes that the lymph nodes involved with cancer are in the pelvis, and not throughout the body. In other words, my hypothetical cancer is still somewhat isolated at this point.

What is the rationale for this approach?

This recommendation logically follows several steps:

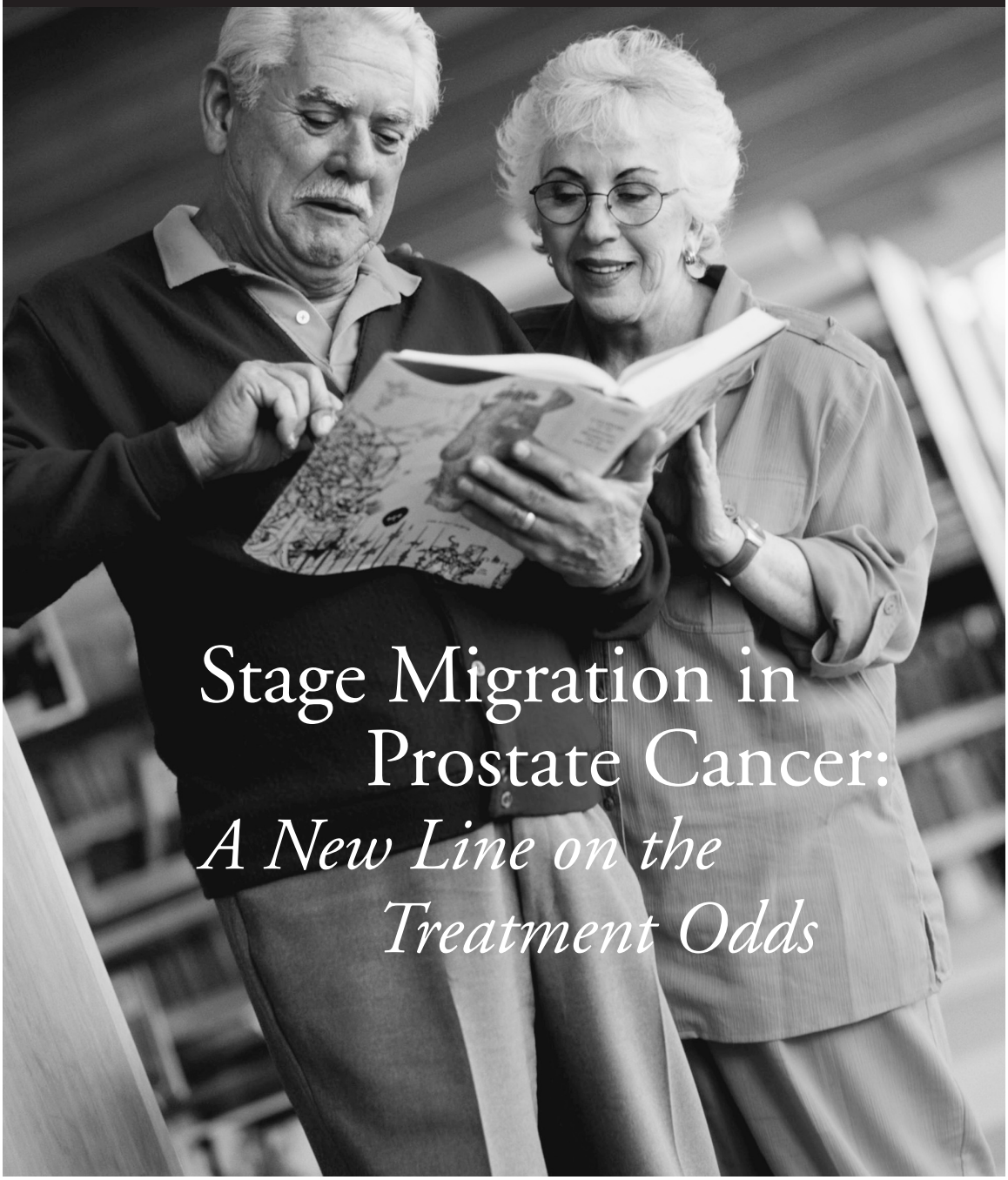
1. Assuming that the spread of prostate cancer is a systematic, stepwise process—it starts in the prostate gland, spreads to lymph nodes, and then to bones, lungs and other organs—then there should be a window of time in this metastasis process when the cancer has spread to the lymph nodes, but has not yet gone beyond. If that is the case, by treating the cancer which is confined to the prostate and lymph nodes, we have a chance for cure. (In some cases, cancer spread may not be so predictable from prostate, to lymph nodes, to bones and lungs.)
2. Even if some cancer has spread beyond the lymph nodes (but is too small to be detected with currently available tests such as a bone scan, chest X-ray or liver CT), the number of cancer cells outside of what could be treated with radiation therapy is probably few. (If there are more than a limited number of spread cancer cells, then bone scan, CT and other tests should have identified these spots of cancer.) Further, these stray cancer cells may commit suicide through the process of apoptosis because of the hormone therapy. (See Chapter 7.)
3. Even if all cancer cells are not killed by the current treatment, at least the therapies will decrease the number of cancer cells living in the body. After treatment, they will then take longer to grow back to a large size than if we do nothing. Without any treatment, the number of cancer cells is much higher to start with, and will continue to grow even more.
4. The bulk of the cancer cells are located in the pelvis, making it an easy target for radiation therapy.

What if lymph node involvement has spread beyond the pelvic region?

If the lymph nodes in the abdomen or lower neck (above the collarbone, called the "supraclavicular region") are involved with cancer, then the cancer is far more advanced and calls for different treatment options. At this point, treatment options include:

- Hormone therapy.
- Radiation therapy.
- Hormones plus radiation.
- Chemotherapy.
- Investigational therapies through clinical trials.
- No treatment if there are no bothersome symptoms.

Chapter 13



Stage Migration in Prostate Cancer: *A New Line on the Treatment Odds*

When trying to predict an individual's odds of conquering cancer, physicians often look at historical treatment results for large numbers of patients who had similar conditions. For example, the physician knows that men with stage T_{1b} prostate cancer will respond better to treatment than those with stage T_3. However, the phenomenon of stage migration can alter the physician's perspective.

What is stage migration?

Since the PSA test (see Chapter 2) was introduced in 1987, cancers detected only by PSA have increased significantly, while the number of advanced cancers has decreased. This is called "stage migration," the phenomenon whereby PSA screening has caused a significant down-staging of the disease. You will find references to this in other prostate cancer literature, and a few of my papers discuss this (see references, Jani 2001 and Vijayakumar 1998). Because of stage migration, the national death rate from prostate cancer has decreased significantly. In other words, more patients are coming to their doctors for treatment when their prostate cancer is still potentially curable.

As an example of stage migration, let us assume that there are only two stages of cancer: "early" and "late." Let's also assume that there are 50 patients with early stage cancer, and they live for 10 years after diagnosis; and there are 50 patients with late stage cancer, and they live for five years after diagnosis. Now, suppose a new test is developed that is more sensitive and more accurate than previous tests. The new test determines that 10% of the early-stage patients are actually late-stage patients. With this new test, we now have 40 early-stage patients and 60 late-stage patients. The 40 early-stage patients will live, on average, about 10 years. But, what about the 10 people previously diagnosed as early stage but now considered late stage with the new test? These people are now a subset of the late-stage patients: their cancer is more advanced than the early-stage group, but less advanced than the other 50 people in the late-stage group. Thus, the physician may predict the longevity for these 10 "new" late-stage patients as being more than five years, but less than 10. [Figure 20]

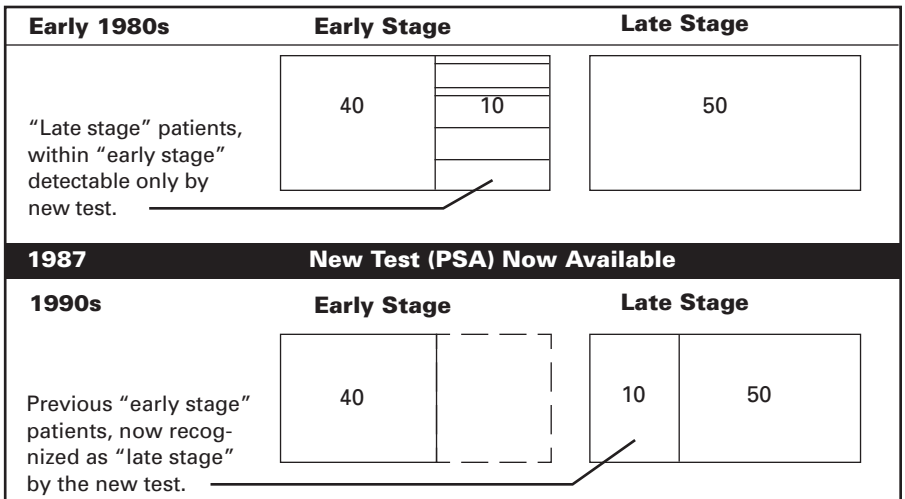
What is the standard test for prostate cancer?

A PSA test combined with a DRE is the standard test for prostate cancer screening. The PSA test can diagnose prostate cancer at an earlier stage than previous tests could. Therefore, more men are being diagnosed with prostate cancer, and the cancer is being found at an earlier stage.

Figure 20 **Stage Migration**

Pre-PSA Era	Early Stage	Late Stage
	Number of cancer cells in an average patient = 10,000,000,000 (1 followed by 10 zeros)	Number of cancer cells in an average patient = 10,000,000,000,000 (1 followed by 13 zeros)
1987	**PSA Test Available**	
PSA Era	**Early Stage**	**Late Stage**
(mostly late 1990s)	Number of cancer cells in an average patient = 100,000,000 (1 followed by 8 zeros)	Number of cancer cells in an average patient = 100,000,000,000 (1 followed by 11 zeros)

For every 100 patients with prostate cancer



The definitions of "early" and "late" stage prostate cancer have actually shifted. Before PSA testing, the average patient with early-stage prostate cancer had 10,000,000,000 (1 followed by 10 zeroes) cancer cells; the average late-stage patient had 10,000,000,000,000 (1 followed by 13 zeroes) cancer cells. Today, PSA tests can identify cancer while it is smaller. Now, we define the average patient with early-stage prostate cancer as having 100,000,000 (1 followed by 8 zeroes) cancer cells, and the average late-stage prostate cancer with 100,000,000,000 (1 followed by 11 zeroes) cancer cells. **(Note: these are hypothetical numbers, to illustrate the comparison.)**

Note that the use of PSA for prostate cancer screening is quite controversial, because it is not known if the PSA test saves lives. A PSA test can detect a small tumor, but this does not necessarily lower a man's chances of dying from prostate cancer. Some tumors may never threaten a man's life, and the testing and treatment for prostate cancer can have significant side effects.

What's the bottom line on all this?

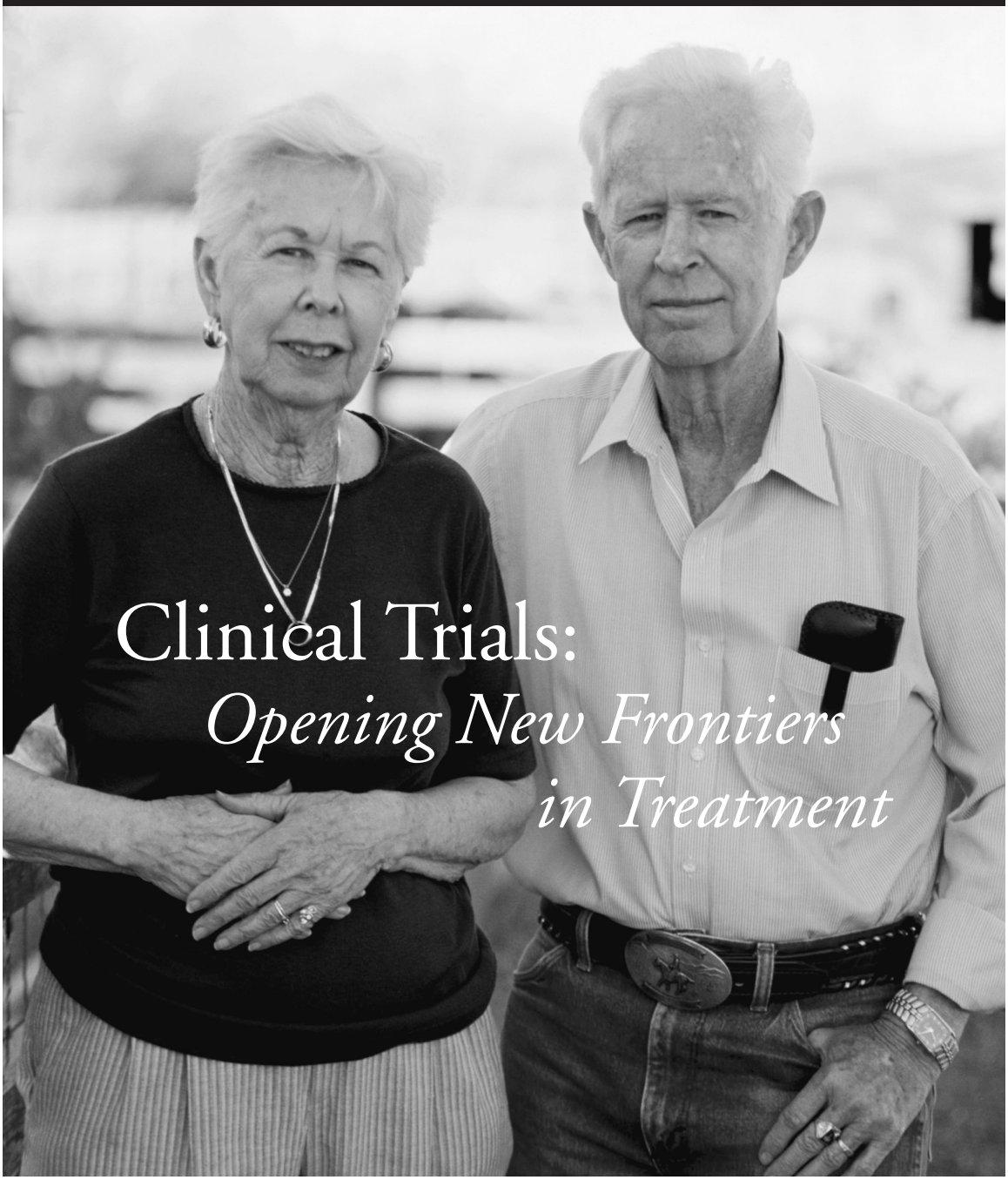
Thanks to stage migration, improved radiation therapy, fine-tuned surgical techniques, new evidence in favor of neoadjuvant hormonal treatments, and other treatment innovations, the paradigm in prostate cancer treatment has shifted in a positive direction. All treatment concepts should be given a fresh look and renewed attention. In general, the chances of being cured are better today than ever before as cancers are being caught earlier and treatments have become more effective. On the other hand, we also run the risk of treating some patients who do not truly require treatment.

How does this stage migration affect prostate cancer outcomes?

Previous tests could not detect the earliest stages of prostate cancer. Today, because more prostate cancers are being diagnosed very early, the overall chances of cure are probably better now than in the past. (However, this has not yet been documented. We do know that most cancers—when diagnosed at an early stage—have a better chance of being eliminated than the same type of cancer when diagnosed at a later stage.)

Because many cancers are now diagnosed earlier, the findings of older studies are no longer relevant for predicting today's outcomes. Why? This is because, in many cases, therapies are being applied to cancers that are truly less advanced than treated cancers were in the past.

Chapter 14



Clinical Trials: *Opening New Frontiers in Treatment*

What are clinical trials?

Clinical trials—also called "clinical studies"—are monitored, structured tests that evaluate the safety and effectiveness of new therapies. These trials use actual patients. Often, these trials are overseen and funded by a governmental body, such as the National Cancer Institute (NCI) or National Institutes of Health (NIH).

The words "clinical trial" make it sound so official and bureaucratic. Yet, trials do not necessarily have to mean something sinister. The first human being was probably the first clinical trialist: he or she tried some plant, herb, fruit or seed with a curiosity to see whether it healed, cured or relieved a condition.

We human beings have not stopped being clinical trialists since those earliest days.

Today, a clinical trial is a carefully planned scientific study—a research endeavor—designed to answer questions of importance to human health and for remedying disease. These questions can only be answered by carefully conducted studies on human subjects. The term "clinical" implies that the study involves actual observation of people; in contrast to research that is done in a laboratory or by evaluating pre-existing data.

Because they require using unproven therapies on humans, clinical trials are designed carefully, with thought, compassion and stringent ethical standards.

Is there preliminary testing before the new therapy is used on people?

Yes, there usually is preliminary testing of a new therapy before it reaches humans. Typically, researchers work in laboratories to substantiate their theories that a new drug or treatment approach has a likelihood of being effective against a particular disease. Many clinical ideas—new thoughts to improve human health—actually begin in a laboratory, often by serendipity.

Once an initial observation on a drug is made in a laboratory, the new drug is tested first on cells in test tubes and petri dishes; then on small mammals like mice; then on larger mammals. Finally, once its safety has been reliably confirmed among animals, the new drug is tested in human subjects.

There are attempts to skip these steps of testing with animals. If this could be accomplished, experimentation on animals could be spared. Significant progress has been made in the humane treatment of animals used for medical research.

Before they reach human subjects, each of these studies has to be approved by an individual hospital's Institutional Review Board or Ethics Committee, which is composed of scientists, physicians, lawyers and the lay public. In all studies, patients have to be informed about the experimental nature of these studies prior to the start of a new treatment approach. The researchers must obtain the person's consent before including him in a study.

What are the clinical trial steps?

Once they reach humans, clinical trials often go through three phases: I, II and III.

Phase I:

The patients who agree to participate in Phase I studies are the noblest of noble people. They have consented to participate in a study of new interventions and inventions which are being used in human subjects for the first time. What brave souls these patients are! They are pioneers in their own right.

Patients who participate in Phase I studies often have terminal illnesses; probably no treatment or standard intervention is available to them. When the Phase I trial begins, the side effects and complications of the new drugs or treatments are still unknown. Phase I trials focus on finding the maximum tolerable dose of a new drug, determining the best way to administer it, and identifying any major side effects or toxicities. Phase I trials help determine the safety of a new therapy, and usually include only a small number of people.

If no serious complications are seen in Phase I studies, and the dose and route of giving the drug (by mouth, by injection, etc.) are determined, the new drug or treatment goes to Phase II. Nine out of 10 new ideas never get past the Phase I stage.

Phase II:

In Phase II clinical trials, the usefulness of the new treatment or drug is refined further. Phase II cancer trials attempt to define which types of tumors are most sensitive to the investigative therapy, and whether the therapy is, in fact, effective.

The patients who participate in Phase II studies usually have advanced cancer, but not necessarily terminal illness. Phase II studies usually include more people than Phase I, but still a relatively small group. The type and stage of the disease are often similar among all the patients who participate in such a study. In a Phase II

study, one looks for the following:
- How good is the new treatment?
- What are the major complications?
- Is it safe?
- Does it have the potential to be better than a standard treatment?

If the new idea gets passing grades in Phase II studies, it reaches the Phase III stage.

Phase III:
Phase III studies can involve hundreds or even thousands of people, often in multiple medical centers around the country. In Phase III studies, head-to-head comparisons are made between the new promising idea, treatment or drug versus the old, established, standard treatment. Patients with similar stages of the same disease who have comparable health status and are the same gender are randomized: half take the standard treatment or a placebo (which has no therapeutic effect), half take the experimental treatment. (Randomization is like tossing a coin. One has equal chances of getting the old or the new treatment. Neither patients nor their physicians have any control over this "coin toss"; a computer does the randomization so that any chances of bias or preferential treatment are removed.) In a "blind" study, the participants do not know which treatment they are taking. Phase III trials are stopped if it is clear that one group is having much better results than the other or if the side effects of the treatment prove to be too severe.

Participants in Phase III studies derive two benefits:
1. They have about a 50% chance of getting a new, more innovative treatment. (The investigational therapy may produce worse results than the standard treatment does. However, generally, if a new idea has withstood the scientific scrutiny to reach the Phase III stage, it is likely that its results are at least as good as those with the standard treatment.)
2. Participants gain the satisfaction of having helped to answer an important medical question and having helped their fellow human beings to potentially obtain new, more effective therapies.

Where can a patient find clinical trials?
Typically, Phase I and Phase II clinical trials are available only through academic medical centers or other leading cancer institutions. Phase III trials may be available to prostate cancer patients through community hospitals, as well as the academic medical centers and other leading cancer centers.

You can get a list of current clinical trials by calling the National Cancer Institute's Cancer Information Service toll free at 1-800-4-CANCER or visiting the NCI clinical trials Web site (www.cancer.gov/clinical_trials). Your doctor can also give you information on clinical trials happening in your area. For example, at U.C. Davis Cancer Center, information on clinical trials open currently can be found at www.ucdmc.ucdavis.edu/cancer and choose "clinical trials" from the main menu.

Can a patient withdraw from a study after signing up?

Yes. Patients sign up for the study voluntarily, and can withdraw at any time, for any reason.

Why discuss clinical trials in a prostate cancer book?

Because there is greater need for clinical trials in prostate cancer. For some reason, the number of well-designed clinical studies in prostate cancer is smaller than other cancers such as breast cancer. Further study would help men make good decisions about their treatment options, and could bring newer, more effective therapies to the medical mainstream.

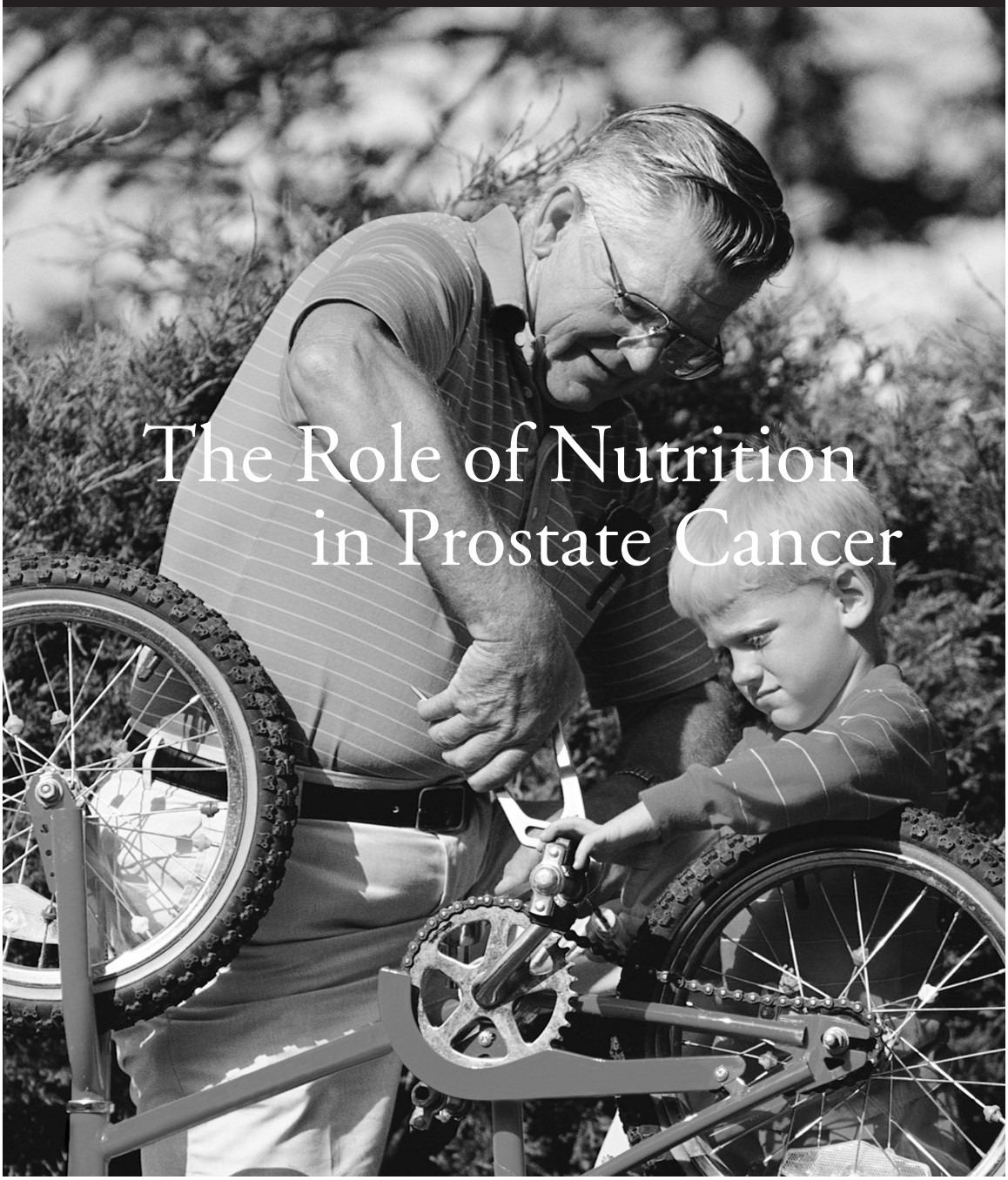
For example, radiation therapy and surgery—the two most important treatment modalities or treatment options—have never been satisfactorily tested head-to-head, although most experts agree that their results are equal. Also, a clinical trial to determine the usefulness of radiation therapy after inadequate surgery has been languishing for many years because not enough patients have signed up to participate.

> This chapter is meant to be a plea. If possible, if there is an opportunity and it is appropriate for you, please help your fellow men by participating in clinical trials. Men with any stage of prostate cancer can choose to participate in a clinical trial. Talk to your doctor to find out if this is an option.

But, only consider a clinical trial after you have:

- Thoroughly read the study protocol and consent form.
- Discussed your participation with your family.
- Thought about it and now feel comfortable with the design of a particular study.
- Asked questions about the study and received satisfactory answers.

Chapter 15



The Role of Nutrition in Prostate Cancer

A nutritious diet can be your ally against cancer, whether you are a cancer patient or not. For men without prostate cancer, healthy eating may be able to lessen their chances of getting it. The American Cancer Society recommendations that follow below are for you.

There is some evidence that diet may play a role in cancer, along with whether or not you smoke and get exercise. For example, a high-fat diet has been associated with higher incidence of cancers of the prostate, breast and colon. *However, further research is needed on the role of diet in developing cancer.*

It is known that people in economically more developed countries have a higher incidence of prostate cancer. However, it is not known whether this difference is due to variances in dietary habits or other factors such as environment, industrialization or physical activity. On the other hand, men in countries with typical diets high in vegetables and low in fat (such as Asian countries) have a lower incidence of developing prostate cancer.

So, what do we know about food and cancer?

Certain foods may contribute to the development of some cancers, either in the steps of initiation, promotion or progression of the cancer. Scientists agree that these three steps are needed for cancer to develop:

Step 1: Initiation.
Cancer cells are abnormal cells. For normal cells to become cancer cells, they need some sort of "trigger" factor. There are many types of triggers, including genetic factors, a carcinogen (such as a chemical in the workplace, the diet, or tobacco), excess radiation, or a change in hormonal status.

Initiation is like putting the key in a car's ignition and turning it to "start."

Step 2: Promotion.
Even after a cancer cell has formed, it could remain dormant and cancer would not develop. Some factor or factors must be present for the abnormal cell to accelerate to the next step and begin multiplying.

In the car analogy, promotion is like engaging the gear from "park" to "drive."

Step 3: Progression.
In cancer, progression occurs as the cancerous cells continue to multiply and create a tumor. Further progression occurs as the cancer spreads to other parts of the body.

In the car, progression occurs when you remove your foot from the brake pedal and press the gas pedal and start traveling to places.

How can diet affect your risk of developing cancer?

Different dietary factors may play a role: types of foods eaten, preparation methods, portion size, variety of foods ingested, and caloric balance.

If diet may play a role in developing cancer, can it play a role in preventing cancer?

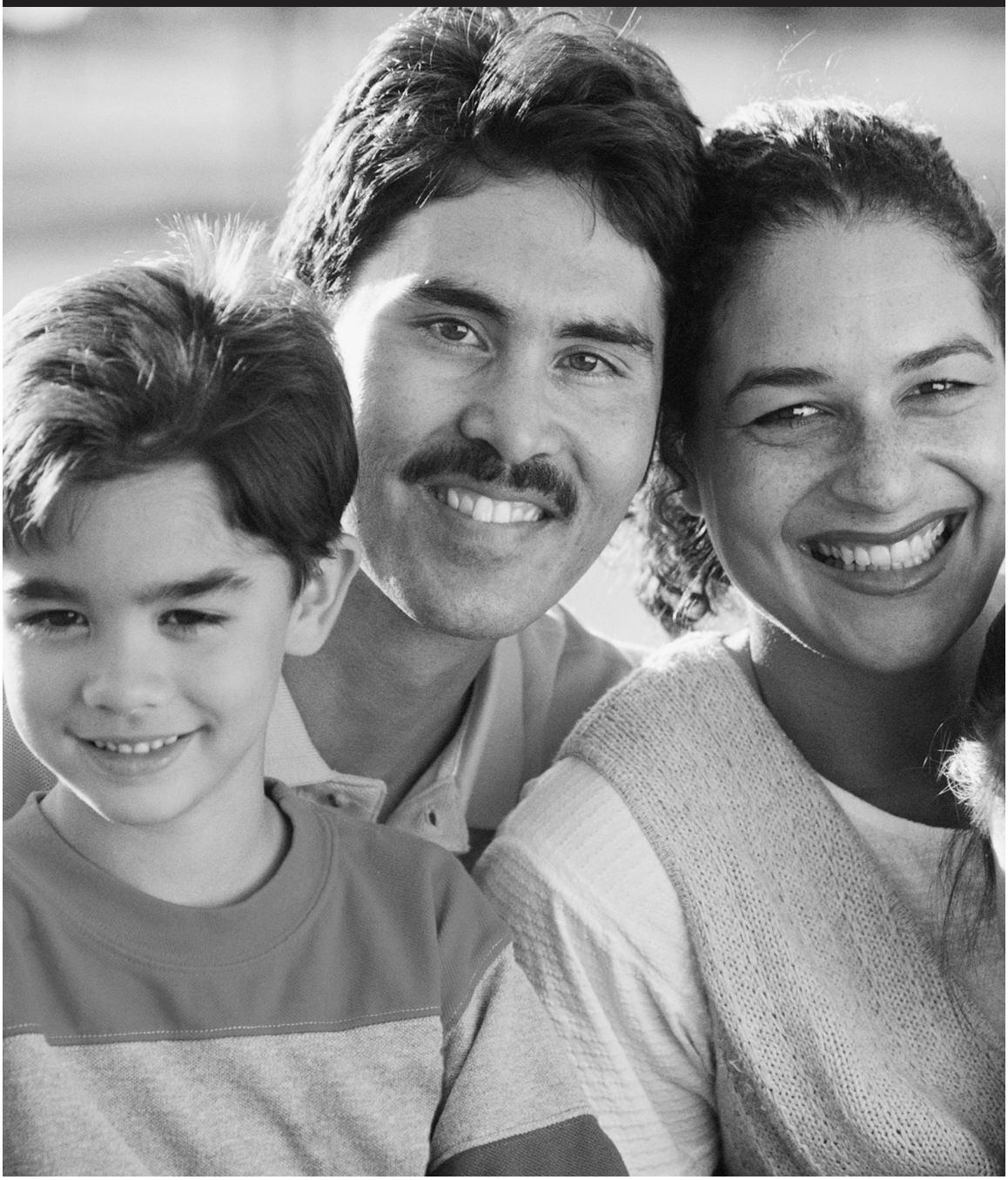
Maybe. The American Cancer Society offers guidelines on diet and nutrition which may help to prevent some cancers.

American Cancer Society Guidelines

1. Eat a variety of healthful foods, with an emphasis on plant sources.
- Eat five or more servings of a variety of vegetables and fruits each day.
- Choose whole grains in preference to processed (refined) grains and sugars.
- Limit consumption of red meats, especially those high in fat and processed.
- Choose foods that help maintain a healthful weight.
2. Adopt a physically active lifestyle.
- Adults: engage in at least moderate activity for 30 minutes or more on five or more days of the week; 45 minutes or more of moderate-to-vigorous activity on five or more days per week may further enhance reductions in the risk of breast and colon cancer.
- Children and adolescents: engage in at least 60 minutes per day of moderate-to-vigorous physical activity at least five days per week.
3. Maintain a healthful weight throughout life.
- Balance caloric intake with physical activity.
- Lose weight if currently overweight or obese.
4. If you drink alcoholic beverages, limit consumption.

Source: American Cancer Society's Website: www.cancer.com. Reproduced with permission.

Conclusion



Thank you for reading this book. My hope is that I have answered some of your questions in a manner that is clear and easy to comprehend. Unfortunately, there are no clearly defined directions for approaching prostate cancer. Each man must decide for himself which is the best course to sail—after reading as much as possible, asking questions of the physicians, and speaking with other men who have been through this experience.

Please note that I have simplified concepts for easier understanding. I have also taken a writer's liberty in selectively presenting information to explain my arguments. All prostate patients should confer with their physicians when deciding on the best treatment choice for them. This book is merely a guide to help you understand more about prostate cancer and to help you make an informed decision with your physician. I encourage you to seek out some of the reference sources listed at the end of this book.

Good luck on the journey back to health.

Dr. Vijayakumar

Resources

Glossary

Adjuvant therapy: A treatment added to your main treatment. For example, this could be radiation, hormone therapy, or chemotherapy done after surgery to destroy any cancer cells that may remain.

Advanced cancer: Cancer that has spread beyond the prostate to surrounding structures or to other parts of the body.

Androgen: A male sex hormone, such as testosterone, that produces male characteristics (facial hair, deep voice). Prostate cancer cell growth is stimulated by testosterone.

Anti-androgen: type of drug that blocks the effects of an androgen

Benign: Not cancerous. A tumor can be benign.

Benign prostatic hyperplasia (BPH): Enlargement of the prostate gland, which occurs as a natural result of aging. BPH is not cancer. However, it can mimic some of the same symptoms as prostate cancer, such as enlarged prostate and higher PSA level.

Biopsy: A small sample of tissue that is removed from the body and examined under a microscope to see if cancer cells are present; also the procedure of removing this sample.

Bladder: The balloon-shaped organ that holds urine temporarily before it is sent out of the body through the urethra, which passes through the prostate.

Brachytherapy: Internal radiation therapy using an implant of radioactive material, sealed in needles, seeds, or wires, and placed directly into or near the tumor; also called "internal radiation therapy." Also called brachy, interstitial radiation therapy (IRT), or implant radiation. (see chapter 6)

Cancer: An abnormal growth in the body, over which the body loses its control. Cancer cells are generally autonomous. Cancer cells almost always tend to spread. If left untreated, cancer will kill the host.

Capsular penetration: Cancer has invaded the prostate capsule, surrounding the prostate gland. This is a more advanced stage of prostate cancer.

Catheter: A thin, hollow, flexible tube inserted into the urethra going into the bladder to allow the urine to drain, such as in the weeks after a radical prostatectomy.

Chemotherapy (chemo): Treatment with drugs that kill or injure cancer cells.

Core needle biopsy: A procedure to remove cells or tissue from the prostate, using a narrow needle and an ultrasound probe, so that a pathologist can examined them for signs of cancer.

CT scan (CAT scan, computed axial tomography): A diagnostic test linking an x-ray machine and computers to produce cross-sectional images of the body.

Differentiation: Abnormal cancer cells are compared to normal cells under the microscope, and are given a "score" by the pathologist. This scoring of cancer cells into "well," "moderately-well," or "poorly" differentiated is called "differentiation."

DNA (deoxyribonucleic acid): The molecules inside cells in the form of a twisted double strand that carry genetic information and pass it from one generation to the next. Radiation damages DNA in cancer cells.

Dosimetrist: A person who plans and calculates the proper radiation dose for treatment.

DRE: Digital rectal examination. This examination enables the physician to feel the prostate with his finger, and to assess whether the prostate is enlarged or has abnormal (potentially cancerous) growth. (However, early-stage prostate cancer is too small to be felt by hand.)

EBRT: External beam radiation therapy – radiation directed from a source outside the body on a cancer within the body. (see chapter 5)

ED/erectile dysfunction: The inability to have or maintain an erection and a potential side effect of treatments for prostate cancer; impotence.

Fine needle aspiration: A procedure sometimes used to see if prostate cancer has spread to the lymph nodes inside the pelvis; a thin needle is used to draw up samples.

Gleason score or grade, Gleason Sum: A grading system used to help define how aggressive a cancer is. Gleason scores look at the primary and secondary cell patterns. Gleason Score is obtained by adding the primary and secondary Gleason grades.

Hormone: A chemical substance formed in one part of the body and carried by the blood to another part, where it starts and coordinates various body functions, such as growth. Testosterone is the primary male hormone.

Hormonal therapy: Treatments that add, block or remove hormones. (see Chapter 7)

Impotence: Inability to obtain or maintain an erection.

Incidence: The number of persons with cancer among 100,000 persons in a given year, generally for a defined geographic region, for example, the U.S.

Incontinence (urinary incontinence): Inability to control urine flow.

Latent cancer: A latent or insignificant prostate cancer is one that, except for new tests, would not have been found and might not have caused death even if left untreated.

LHRH: A short name for "luteinizing hormone-releasing hormone," a hormone that affects testosterone levels. LHRH can be made artificially to suppress the production of testosterone by the testes. LHRH agonists are sometimes used to treat prostate cancer. Medical castration is performed with LHRH analogs, instead of performing surgical castration.

Linear accelerator: A machine that creates high-energy x-rays to treat cancers, using electricity to form a stream of fast-moving subatomic particles; also called a "linac".

Localized: Cancer that has not spread beyond the initial organ (the prostate).

Lymph nodes: Lymph nodes, also called lymph glands, are small, oval or round bodies, most prominently in the armpit, neck and groin areas, that contain immune system cells that help fight cancer and other infections. Analysis of the lymph nodes can help determine the cancer stage since some of them are located close to the prostate.

Malignant: Cancerous.

Metastasis, metastasize, metastatic: Refers to the spread of cancer from its primary location (the prostate) to other parts of the body. Prostate cancer often metastasizes to the bones and lungs.

MRI (magnetic resonance imaging): A diagnostic test in which a magnet is linked to a computer to produce detailed images of parts of the body.

Neoadjuvant: Treatment that is given before the primary treatment (generally radiation or surgery) in order to improve the success of the main treatment. Examples are chemotherapy, radiation therapy, and hormone therapy.

Nomogram: A mathematical model, such as the Partin tables for prostate cancer, that takes variables such as PSA, Gleason score, and clinical stage, and predicts the likelihood that cancer has spread to the lymph nodes or other organs.

Oncologist: A doctor who specializes in treating cancer.

Orchiectomy: castration; surgical removal of the testicles, the major source of male hormones.

Pathologist: A doctor who specializes in identifying diseases by studying cells and tissues under a microscope.

Percent free PSA: A blood test that determines how much PSA circulates unbound in the blood and how much is bound together with other blood proteins. If your PSA is between 4 and 10, a low percent free PSA (25% or less) suggests that prostate cancer may be present and so a biopsy may be needed.

Perineum: The region between the scrotum and the anus in males.

Placebo: An inactive substance, often used in clinical trials. To compare the effectiveness of an experimental treatment, one group of test subjects will receive a placebo; another will receive the medication being tested.

Prognosis: A prediction of the probable outcome of a disease, especially the chances of recovery from it.

Prostatitis: Inflammation of the prostate that can create problems with urinating because the prostate swells around the urethra. Prostatitis is not cancer.

Proton: A small, positively charged particle of matter found in the atoms of all elements. Streams of protons generated by special equipment can be used for radiation treatment.

PSA: Prostate specific antigen. Cells in the prostate gland produce this substance. Prostate cancer cells produce PSA at a much higher rate than healthy prostate cells do.

PSA density: A test that is done after TRUS and is determined by dividing the PSA level by the size or volume of the prostate. A high PSA density suggests a greater chance of having prostate cancer.

PSA test: A diagnostic test used to measure the level of PSA in the bloodstream. Elevated PSA can indicate cancer.

PSA velocity: A test that tells how quickly the PSA level increases over a period of time, generally three measurements over an 18-month period. A PSA velocity over 0.75 ng/ml per year is high and suggests that it is possible that cancer is present – even though the total PSA level is normal – and indicates that a biopsy is needed.

Radiation: Energy carried by waves or a stream of particles.

Radiation Oncologist: A doctor who specializes in treating cancer with radiation.

Radiation Physicist: The specialist who makes sure that the radiation machine delivers the right amount of radiation to the treatment site. In consultation with the radiation oncologist, the physicist also determines the treatment schedule that will have the best chance of killing the most cancer cells.

Radiation therapist: The person who runs the equipment that delivers the radiation.

Radical prostatectomy: Surgical removal of the entire prostate gland.

Radiotherapy: Treatment of cancer with x-rays or radioactive substances; also called radiation or radiation therapy. (see chapters 5 and 6)

Recurrent disease: Cancer that has come back after all visible tumor had been eradicated. If it recurs in the area of the primary tumor, it is locally recurrent. If cancer recurs as metastases, it is called a distant recurrence.

Seminal vesicles: Two small pouches behind the bladder and next to the prostate that store semen.

Simulation: The process used to plan radiation therapy so that the target area is precisely located and marked.

Stage of a cancer: Tells how "early" or "advanced" the cancer is, especially whether the disease has spread from the original site to other parts of the body, based on diagnostic tests and a physical examination. Most cancers are categorized as stage T_1/I(A), or T_2/II(B), or T_3/III(C), or T_4/IV(D). Stage T_1 is an early cancer; stage T_4 is a very advanced one.

Testicles: Male reproductive glands located inside the scrotum, behind and below the penis, which produce sperm and the male hormone testosterone.

Testosterone: The main male hormone, most of which is produced in the testicles, that promotes the growth of male secondary sexual characteristics. In men with prostate cancer, it can also encourage growth of the tumor. It comprises about 90 percent of the androgens in a man's body. Halting the production and conversion of testosterone is the primary objective of hormone therapy.

TRUS (transrectal ultrasonography): A test using sound wave echoes made by a device inserted into the rectum to make a picture of the prostate.

Tumor: An abnormal growth of tissue. A tumor may be cancerous ("malignant") or non-cancerous ("benign").

TURP (transurethral resection of the prostate): Surgery for the treatment of BPH (non-cancerous enlargement of the prostate), in which an instrument is inserted through the urethra in the penis to cut away non-cancerous prostate tissue. Only part of the prostate is removed. TURP can also be used to relieve symptoms caused by a tumor (it does not cure cancer).

Urethra: The tube running through the penis through which urine is sent out from the bladder and semen is ejaculated in men.

Urologist: A doctor who specializes in diseases of the male sex organs and urinary systems of both men and women.

Reference Sources

Internet Resources

Some Internet information is reliable and trustworthy. However, a lot of internet information is inaccurate and biased. You should talk to your doctor about any cancer information you find on Web sites. Consider, for example, who owns the site? For-profit businesses may not give unbiased information. A site's Web address will tell you what type of organization owns it. For example, addresses ending in "gov" are government agencies; "edu" means an educational institution; "org" is used by non-profit organizations; and "com" is used by businesses. Many search engines purposely place sponsor sites at the top of their results list, so beware when searching. Also ask, what are the qualifications of the people who are running the site? How current is the information? Many websites are not updated regularly. Avoid any site that asks for a fee for information, or that asks you for more information than a user name and password. And I must offer one more caveat: Internet sites come and go; the information below is current only as of 2005.

[http://selected address]

1. www.ucdmc.ucdavis.edu/cancer/specialties/radiationoncology.html (UCDMC Radiation Oncology Department)
2. www.cancer.org (American Cancer Society)
3. http://www.ucdmc.ucdavis.edu/cancer (UC Davis Cancer Center)
4. http://cancer.gov (National Cancer Institute)
5. http://www.nlm.nih.gov (National Library of Medicine)
6. www.cancercare.org (Cancer Care, Inc. – non-profit organization)
7. www.yahoo.com/Health/Diseases_and_Conditions/Prostate_Cancer/Organizations (Yahoo Health Directory)
8. www.ameripros.org (American Prostate Society)
9. www.capcure.org (Association for the Cure of Cancer of the Prostate)
10. www.cancerguide.org/prostate.html (Cancer Guide)
11. www.prostatepointers.org (Prostate Pointers)
12. www.oncology.medscape.com (Medscape Oncology)
13. www.ustoo.com (US TOO—Clinical Trials Listing)

14. www.cancernews.com (Prostate cancer news)
15. www.rado.uic.edu/vijay (Dr. Vijayakumar's home page)
16. www.phoenix5.org/menumain.html (Phoenix 5 Organization)
17. www.dfci.Harvard.edu (Dana Farber Cancer Institute; clinical trials)
18. http://cancerhome.com (Cancer Home)
19. www.cpdr.org (Department of Defense Center for Prostate Disease Research)
20. www.prostatecalculator.org (forecasts course of disease)
21. www.library.utoronto.ca/medicine/prostate (Medical Library of the University of Toronto)
22. http://www.prostate-online.com (Virgil Simmons, personal website)
23. http://www.healingwell.com/prostatecancer (Healingwell.com)
24. http://www.prostatescot.co.uk (Scottish Association of Prostate Cancer Support Groups – links to websites in the USA)
25. http://www.orchid-cancer.org.uk (The Orchid Cancer Appeal – information on prostate cancer)
26. http://www.malecare.org (Male Care Inc.)
27. http://www.prostatecancersupport.co.uk (Prostate Cancer Support Association)
28. http://www.pcaw.com (Prostate Cancer Education Council)
29. www.oncolink.upenn.edu (University of Pennsylvania)
30. www.nafc.org (National Association for Continence)
31. www.mayohealth.org (Mayo Clinic Health Information)
32. www.cdc.gov (Centers for Disease Control and Prevention)
33. http://cis.nci.nih.gov (Cancer Information Service, NCI)
34. http://www.psa-rising.com (prostate cancer survivor news and information)

Organizations

1. UCDMC Radiation Oncology Dept., 1-916-734-8252
2. American Cancer Society: 1-800-ACS-2345
3. National Cancer Institute/Cancer Information Service: 1-800-4-CANCER
4. Administration on Aging/National Institute on Aging: 1-800-222-2225
5. US TOO International: 1-800-80-US TOO
6. American College of Radiology: 1-800-227-5463
7. American Prostate Society: 1-410-859-3735
8. American Society of Clinical Oncology: 1-703-299-0150
9. American Society for Therapeutic Radiology and Oncology (ASTRO): 1-800-962-7876
10. American Urologic Association: 1-866-746-4282

Books

1. *Intoxicated by My Illness.* Anatole Broyard. 1992. (A personal account by a literary man who is dying of prostate cancer. This is not about treatment decisions.)

2. *Man to Man: Surviving Prostate Cancer.* Michael Korda. 1997. (Account by a man who had a radical prostatectomy, and about his recovery afterwards. Recovery from surgery has improved since this was written.)

3. *Prostate Cancer: A Non-surgical Perspective.* Kent Wallner, MD; Smartmedicine Press, 2000. (by a radiation oncologist)

4. *Mayo Clinic on Prostate Health.* Michael Blute. 2003. (This discusses not just prostate cancer, but BPH and other health issues.)

5. *Men, Women, and Prostate Cancer: A Medical and Psychological Guide for Women and the Men They Love.* Barbara Rubin Wainrib, Michael Droller, Jack Maguire, Sandra Haber. 2000. (Written by psychologists, it addresses sexual concerns.)

6. *Dr. Patrick Walsh's Guide to Surviving Prostate Cancer.* Patrick C. Walsh, M.D. 2002. (Written by the famous surgeon.)

7. *The Prostate Cancer Treatment Book.* Peter D. Grimm, John C. Blasko, John E. Sylvester, eds. 2003. (discusses seed implants)

8. *Prostate and Cancer: A Family Guide to Diagnosis, Treatment and Survival.* Sheldon Marks, M.D. 2003.

9. *Prostate Cancer for Dummies.* Paul H. Lange, Christine Adamec. 2003. (written by a surgeon who had prostate cancer)

10. *His Prostate and Me: A Couple Deals with Prostate Cancer.* Desiree Lyon Howe. 2002. (woman's point of view; sexual issues.)

11. *A Primer on Prostate Cancer: The Empowered Patient's Guide.* Stephen B. Strum, Donna Pogliano. 2002. (highly recommended)

12. *Seeds of Hope: A Physician's Personal Triumph Over Prostate Cancer.* Michael A. Dorso, M.D. 2000.

13. *The Men's Club: How to Lose Your Prostate Without Losing Your Sense of Humor.* Bert Gottlieb, Thomas J. Mawn. 2000. (one author is a patient, the other his doctor)

14. *The Lovin' Ain't Over: The Couple's Guide to Better Sex After Prostate Disease.* Ralph Alterowitz, Barbara Alterowitz. 1999.

15. *Love, Sex & PSA: Living & Loving With Prostate Cancer.* Robert Hitchcox. 1997.

Related Articles

1. Abdalla I, Basu A, Hellman S. *An evidence-based analysis of the management of localized prostate cancer.* Cancer J 2002; 8:40.
2. Carter CA, Donahue T, Sun L, et al. *Temporarily deferred therapy (watchful waiting) for men younger than 70 years and with low-risk localized prostate cancer in the prostate-specific antigen era.* J Clin Oncol 2003; 21:4001.
3. Catalona WJ, Carvalhal GF, Mager DE, Smith DS. *Potency, continence and complication rates in 1,870 consecutive radical retropubic prostatectomies.* J Urol 1999; 162:433.
4. Catalona WJ, Smith DS. *5-Year tumor recurrence rates after anatomical radical retropubic prostatectomy for prostate cancer.* J Urol 1994; 152:1837.
5. Catalona WJ, Smith DS. *Cancer recurrence and survival rates after anatomic radical retropubic prostatectomy for prostate cancer: intermediate-term results.* J Urol 1998; 160:2428.
6. Choo R, Klotz L, Danjoux C, et al. *Feasibility study: watchful waiting for localized low to intermediate grade prostate carcinoma with selective delayed intervention based on prostate specific antigen, histological and/or clinical progression.* J Urol 2002; 167:1664.
7. Cooperberg MR, Grossfeld GD, Lubeck DP, et al. *National practice patterns and time trends in androgen ablation for localized prostate cancer.* J Natl Cancer Inst 2003; 95:981.
8. Crook J, Lukka H, Klotz L, et al. *Systematic overview of the evidence for brachytherapy in clinically localized prostate cancer.* CMAJ 2001; 164:975.
9. D'Amico AV. *How to compare results after surgery or radiation for localized prostate carcinoma.* Cancer 2002; 95:2041.
10. D'Amico AV, Chen MH, Roehl KA, Catalona WJ, et al. *Preoperative PSA velocity and the risk of death from prostate cancer after radical prostatectomy.* N Engl J Med 2004; 351:125.
11. deVere White RW, Deitch AD, Jackson AG, Gandour-Edwards R, Marshalleck J, Soares SE, Toscano SN, Lunetta JM, Steward SL. *Racial differences in clinically localized prostate cancers of black and white men.* Journal of Urology 1998;159:1979.
12. Fiveash JB, Hanks G, Roach M, et al. *3D conformal radiation therapy (3DCRT) for high grade prostate cancer: a multi-institutional review.* Int J Radiat Oncol Biol Phys 2000; 47:335.

13. Fowler FJ Jr, McNaughton Collins M, Albertsen PC, et al. *Comparison of recommendations by urologists and radiation oncologists for treatment of clinically localized prostate cancer.* JAMA 2000; 283:3217.
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16. Han M, Walsh PC, Partin AW, Rodriguez R. *Ability of the 1992 and 1997 American Joint Committee on Cancer staging systems for prostate cancer to predict progression-free survival after radical prostatectomy for stage T2 disease.* J Urol 2000; 164:89.
17. Holmberg L, Bill-Axelson A, Helgesen F, et al. *A randomized trial comparing radical prostatectomy with watchful waiting in early prostate cancer.* N Engl J Med 2002; 347:781.
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Notes

Notes

Physician Team

I may need the following people to coordinate my treatment and care:

a) My Family Doctor/Internist: _____

Phone: _____ Fax: _____

b) My Urologist: _____

Phone: _____ Fax: _____

c) My Radiation Oncologist: _____

Phone: _____ Fax: _____

d) My Medical Oncologist: _____

(only if my cancer is metastatic or recurrent)

Phone: _____ Fax: _____

e) My Nurse: _____

Phone: _____ Fax: _____

Evaluating the Physician Team:

a)	Do my doctors know each other?	☐ **Yes**	☐ **No**
b)	If not, have the physicians talked to each other?	☐ **Yes**	☐ **No**
c)	Are they team players?	☐ **Yes**	☐ **No**
d)	If they are not already an established team, are the physicians willing to communicate with each other about my care?	☐ **Yes**	☐ **No**
e)	Are my doctors board-certified?	☐ **Yes**	☐ **No**
f)	Are they experienced in treating prostate cancer?	☐ **Yes**	☐ **No**
g)	Do my doctors know the long-term outcomes of their patients? What are they?	☐ **Yes**	☐ **No**
h)	Can I contact a few of their patients? (Do this to learn how they are treated and how they feel about their doctor.)	☐ **Yes**	☐ **No**
i)	What are my treatment options?	☐ **Yes**	☐ **No**
j)	What will happen if I don't treat the cancer?	☐ **Yes**	☐ **No**
k)	Which treatment do you recommend, and why?	☐ **Yes**	☐ **No**
l)	How long will it take to know if the treatment has worked or not?	☐ **Yes**	☐ **No**
m)	What are the side effects, and how long do they last?	☐ **Yes**	☐ **No**
n)	If the treatment fails, what will my options be?	☐ **Yes**	☐ **No**
o)	How can I get in touch with you if I have questions?	☐ **Yes**	☐ **No**
p)	What kind of help will I need at home after treatment, or during treatment?	☐ **Yes**	☐ **No**