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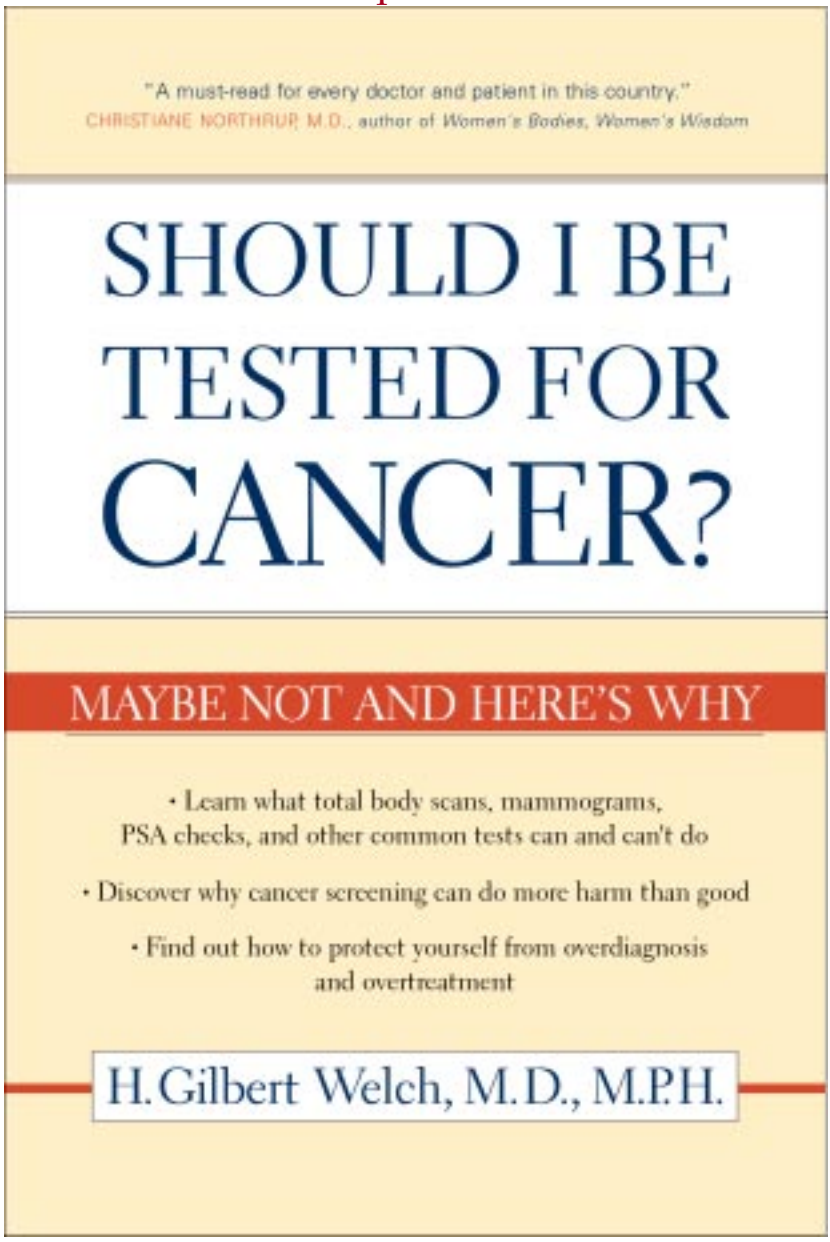


TWO *You may have a "cancer scare" and face an endless cycle of testing*

In our society, information gathering is viewed almost uniformly as a good thing. (It *is* the "information age," after all.) Nowhere is this more true than in medicine. For doctors, more information is always better. In the past, most of our information came from the patient. Now it increasingly comes from machines.

Doctors like tests because we see them as objective and more reliable than our own subjective judgments. We also see tests as something tangible we can offer the patient at the end of a clinic visit. Patients like tests for the same reasons.[1] Ordering a test validates their concerns and promises concrete information—a definitive diagnosis. Sometimes patients even perceive their care as substandard if they are not given some sort of test. While doctors and patients recognize that treatments may have side effects or lead to complications, both tend to view testing as something that can only help. The prevailing attitude seems to be *It can't hurt just to gather a little information.*

Of course, that is not always true. In this chapter I describe the most familiar problem with cancer testing: the test can be wrong. In short, people with abnormal screening tests often don't have cancer. But before they find out for sure, they may have to go through multiple tests—tests that may be unpleasant and that may lead to complications. Throughout

the testing period, they will worry about whether they have cancer. And some may never get a definitive answer. That can hurt a lot.

TRAPPED IN AN ENDLESS CYCLE OF TESTING

Every other week I see patients in the Veterans Administration walk-in clinic, a clinic for patients who either don't have an appointment or don't have a doctor. I recently saw a gentleman who wanted to have his cholesterol tested. He also wanted to talk about PSA screening for prostate cancer. Like many of our veterans, he came into the examination room accompanied by his wife. Both were in their early 70s.

His cholesterol was fine. I asked him what he'd like to know about prostate cancer screening, and he said he wanted to know why there was any debate as to its usefulness. Just by knowing there was a debate, he was further along than many. I said we really didn't know whether it saved lives or not. He said, "What's the harm in trying?" I told him that many older men have elevated PSAs (because of enlarged prostate glands) and yet don't have prostate cancer. But the only way they can find out that they don't have cancer is to have a prostate biopsy (a procedure no one enjoys—more on that later). I also mentioned that some people have indeterminate biopsy results: they won't be told they have cancer, but they also won't be told they do not.

His wife, who had been listening quietly, now spoke up: "It's like ASCUS, isn't it?"

I was stunned. I was talking about the ambiguities of PSA screening for prostate cancer; she thought immediately of Pap smear screening for cervical cancer. It was a remarkable connection, one many doctors might miss. And she was right. ASCUS stands for "atypical squamous cells of unknown significance," which are frequently detected in a Pap smear. It's not cancer, but it's not normal. Instead we call it an "indeterminate" result. I told her the analogy was right on target.

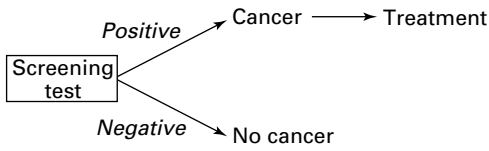
She and her husband then shared what she had been through over the past five years. She had been told that her Pap smear was abnormal. It was then repeated every three to six months. She had had a colposcopy: an optical instrument was placed in the vagina to better visualize the

cervix. She had been biopsied. She had been told she did not have cancer. But the Pap smears were still abnormal. She had had cryocauterization: a cold probe was used to freeze and kill cells on the cervix. She had had laser therapy: a high energy light beam was used to burn and kill cervical cells. Most recently she had had a cervical conization: a procedure in which the core of the cervix is cut out. Her Pap smear was still abnormal.

Some doctors were suggesting that she have a hysterectomy—removal of her entire uterus and cervix—even though they could not prove she had cancer. Others were saying she should just keep checking. Neither approach appealed to her. She was fed up. What she wanted was the answer to an apparently simple question: "Is there a problem or not?"

TESTS ARE IMPERFECT

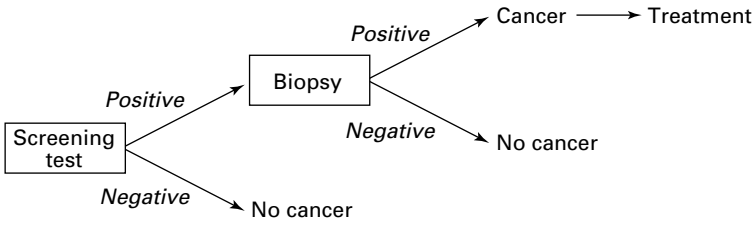
In an ideal world, we'd have ideal tests. They'd be cheap, simple, safe, and quick. And they would never be wrong. Among people who had cancer, the test for cancer would always be positive, while among those who didn't have cancer, the test would always be negative. Positive tests could immediately be followed by early treatment; negative tests would result in immediate reassurance. This utopian ideal would look something like this:



Cancer, however, is a diagnosis made by examining human tissue under the microscope. And the only way to look at tissue under the microscope is to do a biopsy: cut a small piece of tissue and remove it from the body. A biopsy is a small operation, and like any operation, it can be disruptive and painful and can lead to complications. So it's not the kind of test you want to perform on everyone.

The job of the cancer screening test is to determine which patients should

be biopsied. In other words, a screening test is a preliminary test. It is not a test to determine who has cancer; instead, it is a test to determine who should be tested further. So the more pragmatic ideal looks like this:



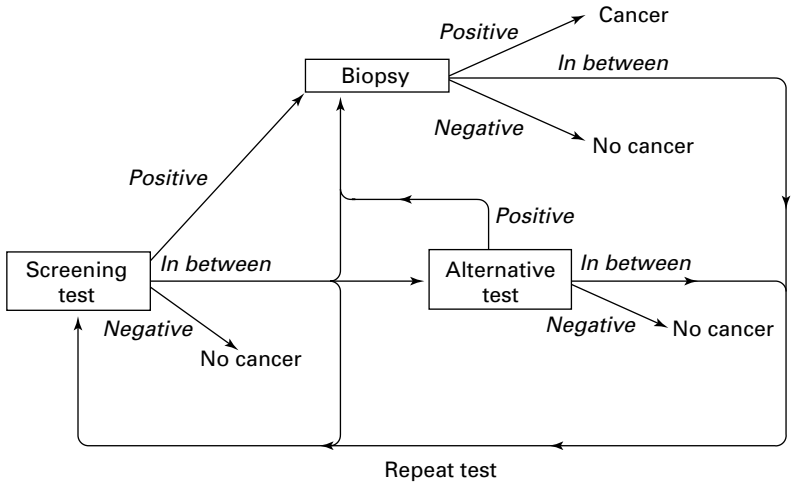
As you may infer from the illustration, a positive screening test can be wrong. That is, a person can be told that his screening test suggests the possibility of cancer, while the biopsy demonstrates that no cancer exists. A positive screening test that is proved wrong is called a false positive. Many call it a "cancer scare."

Can a negative screening test be wrong? The answer is almost certainly yes, although it is very hard to prove. That is because we do not biopsy people with negative screening tests. The only way we ever come to suspect that a negative screening test might have been wrong is when a new cancer becomes clinically obvious soon after a person has a negative test. Recall from the previous chapter the story about my patient's daughter who had metastatic breast cancer diagnosed three months after a normal mammogram. In situations like this, it is reasonable to wonder whether the normal result—or negative screening—was wrong. But as I suggested then, the problem could just as easily be a fast-growing cancer as a falsely negative test. It's impossible to know.

TESTING IN THE REAL WORLD

In the real world, cancer testing is more complex. Test results aren't just positive or negative; often they are somewhere in between. These in-

between results may lead to in-between tests: something more thorough than the screening test but a few steps short of a biopsy. Sometimes in-between results lead to a recommendation simply to repeat the screening test after a few months have passed. The reality, therefore, looks more like this:



Most people will be on the first negative arrow following a screening test: they will avoid this complex cycle altogether.[2] At the same time, a lot more people will be on the positive or in-between arrows than will ever have cancer. False positive and indeterminate results are inherent features of screening—because unfortunately, we don't have perfect tests.

The woman I told you about at the beginning of this chapter has been on every arrow in this figure, except those leading to a definitive diagnosis. You might think of it as a testing cascade, with one test begetting another. Alternatively, you might think of it as being trapped in an endless cycle, where the patient keeps coming back for more testing. Either way it's no fun. What happened to her may not happen often, but it does happen.

Although the testing process differs depending on which cancer is being sought, some features are common to all cancer testing. The screen-

Table 2 Confirmatory testing for abnormal screening result

Screening test (target cancer)	*Early repeat examination*[1]	*Alternative test*[2]	*Biopsy*
Mammography (breast cancer)	yes	Ultrasound	Needle or excisional biopsy
Fecal occult blood (colon cancer)	not recommended	Barium enema; sigmoidoscopy; colonoscopy	Forceps biopsy during sigmoidoscopy or colonoscopy
PSA blood test (prostate cancer)	yes	Ultrasound	Needle biopsy through rectum
Chest X-ray (lung cancer)	yes	CAT scan	Needle biopsy through chest or during bronchoscopy
Pap smear (cervical cancer)	yes	Colposcopy; test for virus	Forceps biopsy during pelvic exam

[1]Typically the screening test is repeated between three months and six months following the initial abnormal screening test.

[2]See the glossary for a description of each of these tests.

ing test itself is generally the simplest, least disruptive, and safest of all the tests used to detect a cancer. When the screening test is abnormal, confirmatory testing is initiated. The confirmatory testing can range from repeating the screening test earlier than normal (in six months instead of one year, for example) to performing an alternative test that is generally more accurate (and generally more involved) to performing a biopsy (the most definitive test). If the screening test is not too suspicious, an early repeat test or an alternative test is often recommended. But if it is suspicious, a biopsy is generally recommended. The confirmatory testing options for common screening tests are shown in Table 2.

HOW COMMON ARE FALSE POSITIVE TESTS?

Now that you know something about the testing process, I want to give you some sense of how often problems occur. I'll start with the false pos-

itive test, or "cancer scare": a positive screening test that, after further confirmatory testing, is determined to be in error. A false positive triggers a process during which people can get hurt, in terms of both their physical and mental health.

The measure of how often a screening test is falsely positive is called a false positive rate: if 100 people are screened and 5 have false positive results, the false positive rate is 5 percent. The false positive rate depends on a number of factors: the test itself, the population being tested, the quality of the testing, and how the test is interpreted. All the common screening tests are plagued by the problem of false positive results.

Mammography

Investigators in Europe have reported false positive rates of about 5 percent for women undergoing mammography for the first time.[3] Women receiving subsequent mammograms were about half as likely to experience a false positive. This is the general pattern with mammography. Here's why: with the first mammogram, the radiologist has no other picture for comparison. All breasts are different, and it is not always clear what is normally different versus what is abnormally different. Without a previous mammogram for reference, therefore, radiologists understandably play it conservative and read more films as abnormal. But with subsequent mammograms there is a point of comparison—an earlier picture of the same breast. Now all the radiologist has to do is look for changes. Something that appeared worrisome in one picture yet is the same in the next becomes a lot less worrisome. So there tend to be fewer false positives on subsequent mammograms.

Investigators at the University of California, San Francisco—who devote particular effort to doing mammography well—report slightly higher false positive rates for first-time exams: about 6 to 7 percent.[4] Following the normal pattern, their subsequent exams then have lower false positive rates. But this is an exceptionally good practice; for the rest of the United States, it appears, the experience is quite different. Some investigators (including myself) have measured what goes on where most patients receive their health care: a typical community practice. Despite the

standard mixture of first-time and subsequent testing, the false positive rate for most American women seems to be much closer to 10 percent.[5] The reason? No one knows for sure, but I suspect that most American radiologists err on the side of calling things abnormal (in part, for fear of being sued), which in turn leads to higher false positive rates.

Prostate specific antigen (PSA)

Now let's consider the blood test for prostate cancer, the prostate specific antigen, or PSA. In September 1993, during "Prostate Cancer Awareness Week," a major effort was made to recruit volunteers for testing. Of the more than 30,000 men over age 50 tested in 148 centers, about 3,000 had an abnormally elevated level of PSA; that is, about 10 percent tested positively.[6] Somewhere between a quarter and a third of these men were found to have prostate cancer, making the false positive rate about 7 percent. Others have reported false positive rates in the range of 7 to 11 percent.[7] The most common cause of a false positive PSA is an enlargement of the prostate gland. Because the prostate tends to enlarge with age, PSAs tend to rise with age. Therefore, false positives are less common in younger men and more common in older men.

The false positive rate for subsequent PSA testing depends on whether the initial result was normal or not. If the men with abnormal PSAs are excluded, the false positive rate for a repeat test drops to around 2 percent.[8] In other words, if your test was normal in the past, you are much less likely to have a falsely abnormal test in the future (which in turn means that an abnormal result in subsequent testing is more likely to represent a cancer).[9] However, if your PSA was abnormally elevated once, it is very likely to remain abnormal in the future—even if you never have prostate cancer.

Fecal occult blood testing

Fecal occult blood testing (in which stool is collected and tested for blood as an early sign of colon cancer) has perhaps the highest false positive rate of any screening test, between 8 and 16 percent.[10] The reason is that there

are many other possible sources of blood: irritation of the stomach, ulcers in the intestine, and hemorrhoids in the rectum, to name a few. The false positive rate is high enough that many doctors try to prepare patients for a false positive at the time of testing. I tend to say something like, "If your test is positive, it doesn't mean you have cancer—it just means we need to look further and see where the blood is coming from." The false positive rate is about the same on subsequent exams.

Pap smears

It is more difficult to talk about the false positive rate for Pap smears because there are two types of abnormal results. First, roughly 10 percent of Pap smears need to be repeated because of inflammatory changes, generally related to infection. Here, age is again an important variable: adolescents have a false positive rate of more than 15 percent, whereas for women over 60 it is less than 5 percent.[11]

Second, around 5 percent of women undergoing a Pap smear will be told they have a cellular abnormality that is potentially worrisome for cancer. This number also varies by age. Among adolescents the proportion of smears diagnosed with ASCUS (atypical squamous cells of unknown significance) or SIL (squamous intraepithelial lesion) has been reported to be as high as 14 percent. Since almost no women with ASCUS and SIL have or will develop invasive cervical cancer, virtually all of these test results can be considered false positives. However, many of these abnormalities end up being treated, so the problem can also be characterized as unnecessary diagnosis.[12] (Though to be fair, the treatment is fairly simple, often consisting of freezing part of the cervix, much as is done for precancers of the skin.)

So there you have it: our four major screening tests—all of which can, and do, render false positive results. (If you want a rule of thumb for the frequency of false positive cancer tests, put it somewhere between 5 and 10 percent.) In fact, a positive screening test is much more likely to be a false positive than a cancer, generally speaking. So if you receive a worrisome screening test result, just remember: chances are good it is incorrect.

CHANCE OF A FALSE POSITIVE OVER TIME

So far all we have been talking about is the false positive rate after a single screening test, whether it's a first test or a subsequent test. In a program of regular screening, however, you are tested over and over again. Each time you undergo a screening test there's a chance that you will have a cancer scare, that is, that your test will be a false positive. Those are the numbers we've just been looking at. But the chance of you *ever* having this problem accumulates over time. Therefore, the more times you are screened, the more likely you are to have a false positive exam.

To get a sense of the problem, let's do some simple calculations. Imagine a test with a false positive rate of 10 percent for both first-time and subsequent exams. Now consider being tested twice. To determine the chance of having at least one false positive result after two tests, we need to ask the complementary question: What is the chance of *not* having a false positive result after being tested twice? The chance of not having a false positive on an *individual* test is 90 percent (100 percent minus 10 percent). The chance of not having a false positive after *two* tests, therefore, is 90 percent × 90 percent, or 81 percent. So what is your chance of having *at least* one false positive? It is 100 percent minus 81 percent, or 19 percent.

Now let's consider 10 years of annual screening. To determine the chance of having at least one false positive result over this period, we need to follow the same procedure, this time asking what the chance is of *not* receiving a false positive after being tested 10 times. The answer is

$$90\% \times 90\% \times 90\% \times 90\% \times 90\% \times 90\% \times 90\% \times 90\% \times 90\% \times 90\%$$

or

$$0.9^{10} = 0.35 = 35\%$$

Looking then at the complementary situation, we find that the chance of having *at least* one false positive over a 10-year period is 65 percent. In other words, in 10 years of annual screening with this test, you are more likely than not to have at least one cancer scare—and possibly a cascade of additional testing as a result.

Table 3 uses this same approach to demonstrate the effect of five (single-

Table 3 Cumulative risk of one or more false positive tests in a 10-year program of screening

	Chance of having at least one false positive over ten years when screened:		
False positive rate for an individual test	Every year	Every two years	Every three years
1%	10%	5%	3%
2%	18%	10%	6%
3%	26%	14%	9%
5%	40%	23%	14%
10%	65%	41%	27%

test) false positive rates and three screening frequencies on the chance of having at least one false positive in a 10-year screening program. As this table shows, the cumulative risk of having a cancer scare can be reduced in two ways: have a test with a low false positive rate or test less frequently.

This calculation, though theoretical, is a simple version of the kind of analysis that screening experts do regularly to determine how often to recommend a screening test. The basic trade-off is between missing cancers in between screening tests, on the one hand, and the burden of testing (false positives and subsequent testing), on the other. More frequent screenings mean fewer missed cancers but a higher testing burden. However, the trade-off varies depending on the cancer involved. Analyses of cervical cancer screening, for example, have suggested that Pap smears can be done much less frequently than most women were probably taught (every three years instead of every year) with little, if any, effect on how many cervical cancers are missed. But the change has a big effect on the burden of testing. This kind of analysis is the major reason that most professional organizations recommend that after two or three normal exams, Pap smears be done every three years.[13]

A few studies have tried to measure the cumulative risk of a false positive test. A study at Harvard Pilgrim (a large Boston HMO) looked at women undergoing mammography over a 10-year period.[14] The false positive rate for an individual mammogram (a mix of initial and subsequent

exams) was found to be 6.5 percent, which is lower than the average rate in the United States. The typical woman had four mammograms over 10 years, and about a quarter of the women surveyed had at least one false positive exam. The authors stated that, of women who get a mammogram every year for 10 years, 49 percent would be expected to have at least one false positive.[15]

A study in Australia measured additional testing following Pap smear screening.[16] The investigators were specifically interested in the long-term risk of colposcopy, a confirmatory test for an abnormal Pap smear. They estimated that at current rates of testing, the typical 15-year-old girl has a 76.8 percent chance of undergoing a colposcopy sometime in her lifetime. Because virtually all (99 percent) of these exams will not identify a cancer, they conclude that the lifetime risk of a false positive Pap smear is over 75 percent.

These two studies provide us with some perspective about the downsides of testing. If you are a woman who follows screening recommendations for breast and cervical cancer, the chances are better than 50–50 that—at some point in your life—you will have an abnormal test result and will have additional testing recommended. Thus, it is more likely than not that you will spend some time worrying about whether you have breast or cervical cancer. This may not matter much to some, but may to others.

Finally, consider the American randomized trial of fecal occult blood testing discussed in Chapter 1.[17] A third of participants had at least one false positive test over 13 years, and as a consequence all underwent a complete evaluation of their colon (i.e., colonoscopy). A number of doctors wonder if the high false positive rate of fecal occult blood testing is the reason it works—in that it sends many people to have the test that really helps, a colonoscopy.

RISK TO PHYSICAL HEALTH

Do screening tests pose any risks to your physical health? While some may be uncomfortable (mammogram, Pap smear) and others unpleasant (fe-

cal occult blood testing), none of the major screening tests themselves pose a serious physical risk. However, screening tests may start a chain of events in which physical harm is possible. One of the reasons false positive tests are cause for concern, for example, is that before patients learn they don't have cancer they often must undergo tests that pose more serious risks. One of the most common—and one that typically involves sharp tools—is the biopsy.

In the past, a biopsy often involved going to the operating room. It was real surgery involving long incisions using knives. Nowadays, biopsies are increasingly performed in less expensive settings such as doctors' offices, radiology departments, and endoscopy suites. And instead of requiring knives, biopsies are performed using needles or forceps (a small jawlike instrument that literally takes a bite of tissue). These less invasive approaches make the process safer and easier, and the patient can usually go home soon afterward.

Nevertheless, complications do occur, and they get worse as biopsies delve deeper inside the body. The complications from a breast or cervix biopsy, for example, are minor compared to the complications from biopsies of the colon or lung. In the colon, the biopsy procedure involves a long flexible scope that can perforate (poke a hole in) the wall of the colon. If that happens, surgery is needed. Biopsies of the lung occasionally cause the lung to collapse. If that happens, a tube needs to be inserted inside the chest to reexpand the lung. Perforated colons and collapsed lungs are rough even for the young. For the elderly and the debilitated, they can be deadly.

Nevertheless, even these deep biopsies are relatively safe. Perforated colons occur in, at most, one-half of 1 percent of colon biopsies, while collapsed lungs occur in about 5 percent of lung biopsies.[18]

That said, it's still no picnic. One of my patients who has a chronically elevated PSA level has undergone multiple prostate biopsies.[19] Let me tell you how they are done. Because the prostate is a long way from the skin—deep in the male pelvis between the penis and the bladder—the easiest way to get a needle into it is through the rectum. A patient lies on his side on an exam table while a condom-covered probe, about the diameter of your thumb, is passed into the rectum (my patient doesn't like this part

at all). This probe produces a picture of the prostate using ultrasound (a radar of sorts—the same technique used to take pictures of babies inside pregnant women). The biopsy needle is passed through the probe and into the prostate. Thus the doctor taking the biopsy can view on a small video screen the path of the needle. A prostate biopsy is a relatively safe procedure; only about 1–2 percent of men suffer a major complication requiring hospitalization. Even so, over half will have some sort of complication—generally bloody urine for several days.[20]

My patient—whom I consider an expert in this area—summarizes the process something like this: getting the biopsy is demeaning, and he's uncomfortable for a few days afterward, but it's not the end of the world. After having gone through this four times, though, he's understandably down on the process. When I last asked him about it, he replied: "I'm not dead yet—but what a rat race!"

A DOCTOR BECOMES A PATIENT

While the cancer testing process doesn't pose a great deal of physical risk, it can be pretty uncomfortable and scary. The chairman of radiology at Emory University recently had the misfortune of experiencing firsthand the kinds of problems that can follow a screening test. It is a story best told in his own words, excerpted from a letter published in a radiology journal.[21]

> What is often missing from radiologists' thoughts is firsthand experience with the clinical drama that follows screening or diagnostic tests. My personal anecdote is an example of the clinical aphorism that the only normal patient is one who has not yet been completely worked up.
>
> It began innocently enough with a negative virtual colonoscopy (which involves a CAT scan) that was requested following my routine annual physical examination. Lurking outside the colon were a kidney mass, a 2 cm liver mass and multiple non-calcified nodules in the lungs. Our observant radiologists saw them all.
>
> Further CAT scans of the abdomen demonstrated that the kidney mass was a cyst. The non-enhancing liver lesion was not. A high-resolution lung CAT scan revealed 7–8 non-calcified nodules in the

lower portion of both my lungs. A previous chest X-ray in 1997 was negative.

The CAT scan–guided liver biopsy was not definitive. A PET scan was negative. After much debate, a video-aided thoracoscopy (fiberoptic exam of the lungs) was performed through the ribs. Three small sections of my right lung were removed after the anesthesiologists had collapsed part of it in order to help the surgeons find the nodules. Thorough evaluation by the pathologists made a definitive diagnosis of Histoplasmosis (a common, often asymptomatic, fungal infection).

I awoke in the recovery room after five hours elapsed time with a tube in my chest, a tube in my bladder, a catheter into a vein near my heart, a catheter into an artery in my wrist, a catheter in my spine (for anesthesia), and was being given oxygen in my nose, shots of heparin, a constant infusion of prophylactic antibiotics, and patient-controlled intravenous narcotics.

Over the next four days, the tubes and potent drugs were slowly removed, but the excruciating pain lingered on. However, the nurses were great, the hospital staff superb, the surgeons were the best anywhere and no untoward events or complications occurred. Most of all the outcome was great.

However, it required two weeks at home with Oxycotin and Percodan (narcotic pain killers) before the pain became bearable and a modicum of strength returned. Now five weeks later things are nearly normal except for rib pain caused by the surgical interruption of the nerves. But we are all happy.

He may have been relieved, but he was also motivated to start asking some hard questions about whether radiologists, with remarkably sensitive imaging tests at their disposal, had gotten too far away from what their patients were experiencing. His story certainly makes one wonder whether they are seeing too much.

SENSE OF WELL-BEING

Many people will say that extra testing, the rare risk of physical harm, and the anxiety of false positive and ambiguous results are a small price to pay for early cancer detection. But that really depends on what the benefits of

early cancer detection are. If there is a substantial life-expectancy benefit, then the twists and turns of the testing process may indeed be a small price to pay. If, however, there is trivial benefit to early cancer detection—or no benefit at all—it would be best to avoid the process.

How you feel about the trade-off depends on who you are. Different people will feel differently about what constitutes a "substantial" and a "trivial" benefit. Different people will also feel differently about extra testing, false positive results, and ambiguous results, and an individual's attitude may change over time and under different circumstances.

Some people even experience a false positive screening test for cancer in a positive way. At first, of course, they may be very scared; but while they wait for the confirmatory test, they use their time to think about cancer and about what's important in life. And there is a tremendous sense of relief when they are told that they don't have cancer.

The psychological implications of a false positive test have been best studied in mammography. Researchers in Pennsylvania surveyed women who had recently had abnormal mammograms but did not, as things turned out, have cancer.[22] Three months after their false positive, 40 percent of the women were worried about breast cancer—but so were 28 percent of women with normal mammograms. So the researchers asked whether worrying about breast cancer affected the women's moods. About a quarter of women with false positives thought so, as opposed to only 10 percent of women with normal mammograms. In this study at least, then, false positives had some negative psychological aftereffects, but not a great deal.

But it is important to remember that all the women in this study were interviewed at a time when there was no ambiguity: they knew that they did not have cancer. Had they been interviewed at a different time—when they thought they might have cancer—they would perhaps have answered the questions differently.

The degree of negative psychologic impact resulting from false positive tests is likely a function of both how often an individual experiences them and how long the period of ambiguity lasts. It may be a very short period, lasting only a few days (or a few weeks) until a definitive answer is given—and if the answer is good news, as in the Pennsylvania study, that period of ambiguity may seem minor, even beneficial. But for others,

definitive answers do not come so quickly, and people may be asked to wait a few months and then repeat the test.

Repeat testing is the most common strategy used following an abnormal Pap smear or an abnormal mammogram. In one study, about 90 percent of women with abnormal mammograms in the Medicare program (women over age 65) had the test repeated. Of these, about half had the repeat test within a month, while most of the rest waited five to seven months.[23] For Pap smears, repeat testing in a few months would be even more common.

For a few patients—the woman with persistently abnormal Pap smears or my patient with a persistently elevated PSA—the ambiguity never ends. The real stressor then becomes uncertainty. These individuals are caught in a seemingly endless cycle of testing: no one has found cancer, but no one can (or will) reassure them that they don't have it. The distressing combination of repeat testing and persistent ambiguity may be enough to push such individuals toward treatment for cancer even though no one has established that cancer is present. Both started the diagnostic process assuming, like most of us, that it could never hurt to look. Now they feel differently: they wonder whether they wouldn't be better off if they'd never been tested in the first place.

SUMMARY

Most of the problems discussed in this chapter are no doubt familiar to you. You probably know people who have had an abnormal screening test—but didn't have cancer. They may have had to undergo multiple tests. They may have even had complications. They probably felt a great deal of relief when it was all over. They may appreciate life more now.

You also may know someone who has suffered from not knowing for sure—someone who has waited, and may still be waiting, for follow-up testing. On this point I am conflicted. I want you to be aware that for some screening tests the best strategy for an abnormal result is to repeat the test after a few months. The downside is obvious: during the waiting period there is ambiguity and, for some, considerable anxiety. At the same time, I believe this "check again later" strategy often is the best way to test for

early cancer. As will become clear in later chapters, having information from two points in time may be the key to sorting the wheat (abnormalities that need treatment) from the chaff (abnormalities that are better left alone).

I hope I've given you some sense of how it can hurt to look for cancer. Again, I want to emphasize that just because it can hurt doesn't mean it will. But if you are considering testing, you must understand that false positive tests, with all their consequences—anxiety, potentially endless cycles of testing, and a small risk of physical harm—are side effects of testing. They may even be reason enough for some to choose not to be tested and even forgo a small life-prolonging benefit. Yet despite being the most familiar problems with screening, they are by no means the most important.