

A SEAT ON THE AISLE, PLEASE!

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The Essential Guide to Urinary Tract Problems in Women

ELIZABETH KAVALER, M.D.



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To my daughter, Sonia, and my parents, Marylou and Franklin.

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Introduction

Hardly a glamorous subject, urinary tract problems in women have become my life's work. But how did I arrive at this decision? Unlike Aphrodite, I did not emerge from the medical school clamshell as a urological surgeon and author. Some autobiographical background is called for.

I grew up in one of the few major cities in America that still has a single-sex public high school for girls. Before attending the Philadelphia High School for Girls, I attended a private all-girls grade school in the suburbs. I transferred to public school in the ninth grade, where I was one of 550 girls in my year. Everyone was female, including the president of the student body, the varsity athletes, the entire marching band, the first chair of the orchestra, the valedictorian, and the editor of the school newspaper.

After graduation, I attended Barnard College, the women's college of Columbia University. Although men attend classes in Barnard and the athletic programs are integrated, Barnard has a distinct place within the University. I had many female professors and advisors. My female classmates majored in physics as readily as they did in economics or English. We had a large number of premedical students with a well-structured mentoring program of women doctors who had all graduated from Barnard. My desire to become a doctor did not surprise my friends or family.

The first coeducational institution that I attended was the medical school of the State University of New York in Brooklyn. Nearly 40 percent of my class was female, and for the first two years, no perceptible differences between the education of the male and female students existed. During the third year, like all American medical students, we spent time in the hospital learning to evaluate and treat patients. The year is divided into specialties, such as internal medicine, surgery, and obstetrics and gynecology. At that time, general surgery tended to be a boys' club. Long, grueling hours spent with the same group of eight or ten students, mostly men, created

strong bonds that tended to exclude the few women on the service. Urology, a surgical subspecialty, was a male bastion.

During my fourth year of medical school, I spent a month on the urology service at the Mayo Clinic, in Rochester, Minnesota. While there, I learned about the urological problems suffered by women. I also became aware that there were very few women urologists. No specialty within the medical profession has fewer women practitioners than does urology. Less than 1 percent of urologists in the United States are women.

I realized that it is a field in strong need of well-informed female physicians. I had found my field: I would go into urology, and focus on women's urological problems. Ironically, the next time I dealt with urological issues specific to women was during my fellowship at UCLA Medical Center seven years later. During my six years of residency, I rarely treated a woman who suffered with one of the problems discussed in this book, but not because female patients did not have these conditions. They did, and still do. Rather, the majority of male urologists in practice did not focus on women's urological conditions.

I was the second woman accepted into the urological training program at Mount Sinai Medical Center in New York City in the history of the department. The first woman completed her residency about eight years before I began. She has never practiced urology. Upon completion of her training, she did a second residency in pathology and became a city Medical Examiner. I had no women role models from whom to learn. No women attending physicians trained me, either during my clinical work or my laboratory experience. I was the only woman in every conference and presentation, unless one of the radiologists attended.

Because of this isolation, I became acutely aware of the difficulties that women face when they are seen by male urologists, who traditionally treat male problems. Of course, most physicians, urologists included, are compassionate and interested in giving their patients excellent care. After all, their wives and daughters are women. But most male urologists do not make an effort to learn and understand female urological disorders. Unless special interest is taken to think about them, little progress will be made on either an individual or a scientific level. That is why specialty training is so important. It is not just the experience that one gets from it, but the focus of one's thoughts and ideas in one specific area.

Upon completion of my chief residency year in urology, I pursued a fellowship in pelvic surgery at UCLA, where I learned about female pelvic-floor problems and was exposed to the creative and complicated reconstructive surgery that can be done to correct these problems. I also realized

how desperate our patients are; desperate for information, for answers, and for education. They flew to Los Angeles from around the world because access to physicians experienced in this specialty was not available near their homes. My choice of medical specialty was validated by the fellowship. During that year, I decided that a book on this subject, written by a committed medical professional, would be helpful to many women.

Over the past 20 years, tremendous social and financial resources have been put into research on cancer and heart disease. As a result of the scientific advances in these areas, people are living longer. Older Americans expect to lead active lives playing golf, traveling, and continuing to engage in sexual relations later in life. Quality of life has taken on new meaning in the recent decade. Male impotence, once rarely discussed or acknowledged as a medical issue, is now taken seriously and treated effectively. With more women physicians treating women patients, we, too, are acknowledging the importance of lifestyle problems in our patients.

This book serves as a guide for women who are seeking treatment for the debilitating problems of the urinary tract for their family members. It touches on disorders that affect millions of women, most of whom have no idea where to turn for help. In many cases, physicians themselves are not familiar with the problems from which many of you suffer. As a clinician and a surgeon, I am committed to understanding my patients' problems and applying the optimal treatment available in order to ease and cure their urinary tract problems. No book addresses urinary tract problems in women exclusively. It is my great hope that this book will enlighten women to better understand their problems and help to ease their embarrassment, anxiety, and suffering. As more women become assertive in discussing their concerns in this medical field, more physicians will respond effectively and, one hopes, empathetically.

I have divided the book into five sections, each of which focuses on one aspect of the urinary tract. The first section reviews terminology and anatomy, as well as which medical specialty to turn to for help for your problems. The second section addresses urinary leakage, of which two main types occur in women: stress incontinence and urge incontinence. Stress incontinence occurs when mechanical stress, or pressure, such as laughing, coughing, or sneezing, causes urine to squirt out of the urethra. The second type of incontinence, and the cause of much embarrassment, anxiety, and discomfort for women who are so afflicted, occurs when the urge to urinate results in leakage before you can get to the bathroom.

The third section deals with pelvic organ prolapse, a condition in which the bladder, rectum, small intestine, or uterus falls into the vaginal

canal. The fourth section reviews the causes and treatments of the painful bladder, including urinary tract infections and interstitial cystitis. The fifth section looks at the effects menopause can have on urological symptoms. Anesthesia and pain control for urological surgery are also reviewed. Finally, a glossary provides easy-to-understand explanations for the technical and medical terms discussed throughout the text.

PART ONE

THE BASICS

The Nuts and Bolts of the Female Pelvis

Normal Anatomy and Physiology

In women, the urinary tract is composed of four organs. From top to bottom, these include the kidneys, the ureters, the bladder, and the urethra. The **kidneys** sit under the ribs in the back. Isolated from the organs of the abdomen, the kidneys are covered in fat and muscle. They filter the blood, reabsorbing the red blood cells and eliminating toxins into the urine. Also producing agents that help with the metabolism of calcium and the production of red blood cells, the kidneys are vital structures. Fortunately, most of us have two of them but we can live normally with only one. If one kidney becomes diseased, it can be removed without any negative impact, as long as the other one is normal.

When kidneys become inflamed, they cause severe back pain and fever. Infections of the kidneys start either in the bladder and ascend into the kidneys, or they begin in the blood and seed the kidneys. Kidney infections are serious. They cause high fevers and require long-term antibiotics for eradication. Fortunately, only 1 percent of bladder infections in women ascend the urinary tract and affect the kidneys. The kidneys are very resilient organs. In an anatomically normal woman, even a severe kidney infection will not cause permanent damage.

After filtering the blood, the kidneys eliminate toxins from the body through tiny tubes called **ureters**. The ureters are conduits through which the urine passes on its way into the bladder. If there is a blockage below the kidneys, the ureters will become dilated and will fill with water. As anyone who has had a kidney stone can attest to when the ureters become dilated, it is excruciatingly painful. A blocked ureter will cause severe, colicky back pain. The most common cause of urethral obstruction is a stone that forms in the kidney, gets washed into the ureter, and becomes stuck in the small-caliber tube.

If the process causing the blockage is slow-growing, the dilation of the ureter may not be painful. If the ureters are blocked by a prolapsed

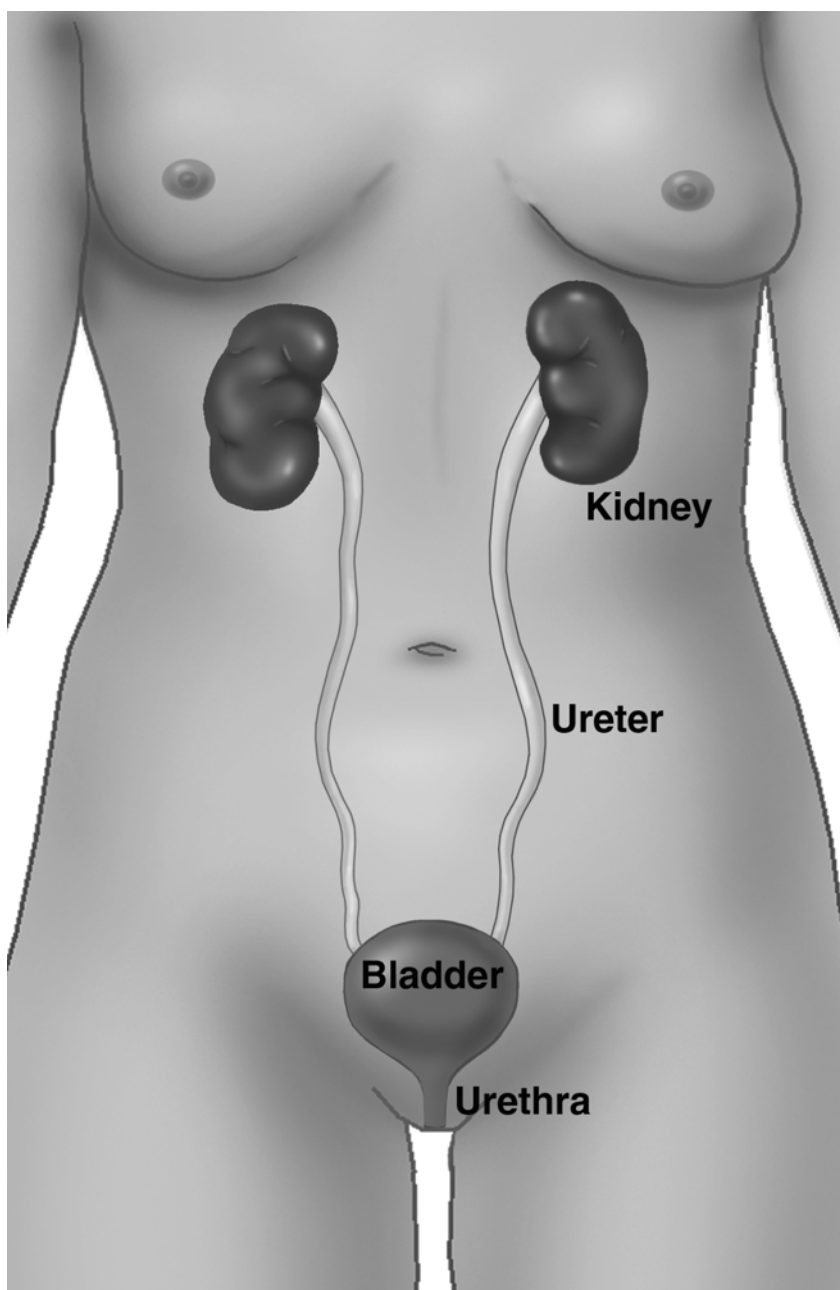


FIGURE 1. *Female Urinary Tract.*

bladder or a mass growing into the ureters, you will not feel pain despite the obstruction. Without special testing, the blockage could go unrecognized. If it is a long-standing obstruction, even with elimination of the causative factor, the ureter will remain dilated. As long as the urine is passing from the kidneys into the bladder, the way the ureter looks is not important.

Finally, the urine enters the **bladder**, where it sits until it is eliminated. Urologists used to think that the bladder was an inactive organ that served only as a holding vessel. However, with more attention being paid to conditions that cause bladder pain, researchers are finding that the bladder is a vital, active organ, with a complex neurological and vascular system.

The urinary bladder (we are not talking about the gall bladder, which is a small sac that sits under the liver and can fill with stones and cause pain) is composed of four distinct layers. The lining is called the **mucosa**. A water-tight system, it protects the inner layers from the toxins that enter the organ. This active layer of cells gets replaced by new cells on a regular basis. Defects in the lining that allow urine to penetrate into the deep recesses of the bladder can cause pain, irritability of the bladder, and frequent urination. Recurrent infections and chronic pain syndromes may possibly be caused by these defects.

The next layer is called the **submucosa** (“under the mucosa”). It is a thin, indistinct layer through which the blood vessels and nerve endings enter and supply the other layers. One can see that if the mucosal layer is imperfect, the urine can easily affect the nerve and blood supply to the bladder since that is the next layer of exposure.

The third layer of the bladder is the real business end of the organ. It is the muscle layer, and is formally called the **detrusor**. The exact character of the muscle is not known, but it does get thick and muscular when it works hard to empty against a resistance, just like the biceps muscle gets larger from weight lifting. However, voluntary control of the detrusor does not seem possible in the same way that we can control our biceps muscle. There is a direct, although subconscious, effect that our brains have on the bladder. In women with certain types of bladder control problems, the detrusor will contract and cause uncontrollable loss of urine if the brain senses cold, anxiety, or proximity to a bathroom. As many of you know, suppression of these impulses is very difficult, making the reaction involuntary but certainly under some sort of conscious control.

The complex detrusor muscle is different from any other muscle in the body in that it can expand to huge proportions (like the uterus) and deflate within seconds (unlike the uterus). It can be controlled by the brain

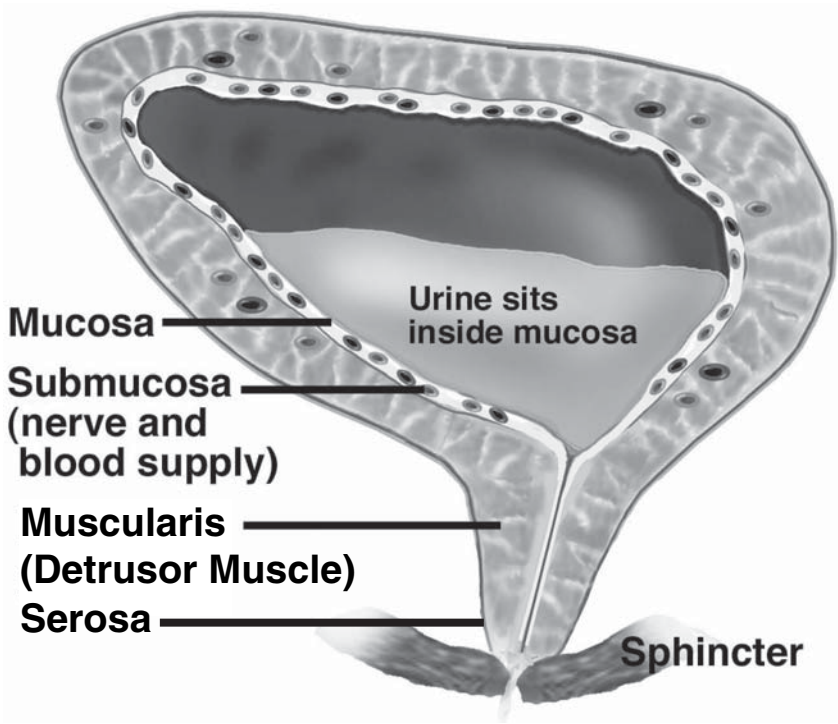


FIGURE 2. *The Layers of the Bladder.*

(voluntary urination) or escape the normal suppressive channels (resulting in leakage). It can thicken due to pushing against a resistance (like the biceps muscle) or it can be thin and paper-like, with no change in symptoms. It can be overdistended and lose its ability to function for weeks or months on end, only to become decompressed and return to normal activity within days. In short, it is quite a resilient muscle that is at the root of many urination problems among men and women.

In women, the detrusor muscle tends to be thin and floppy. Because women don't have prostates to block the flow of urine, they never develop the thick-walled muscle from which men with enlarged prostates suffer. Women suffer from the opposite problem; as a woman ages, her urinary sphincter becomes less efficient, creating less resistance to outflow, often resulting in incontinence. In older women, nothing exists between the bladder and the outside except a very inefficient valve. This is one reason why women suffer from incontinence more than men.

The second reason that men don't develop incontinence is also related to differences in their anatomy. Men have a prostate that supports the bladder (the prostate provides the juice in which the sperm swim around in the ejaculate). Because of that support, and the fact that no empty cavity sits under the bladder (in women, that would be the vagina), a man cannot suffer from a "fallen bladder" (more about that later). So, anatomically, men and women are very different in this area, resulting in different problems requiring different treatments.

The final path of the urine as it leaves the urinary bladder is through the **urethra**. In women, the urethra is only 3 cm long (about 1½ inches); whereas in men, it is about 15 cm long (about 8 inches). This tiny tube sits above the vagina inside the labia. Many women do not realize that the urine comes out of a separate opening. Women have three openings: the urethra, through which urine passes; the vagina, through which a baby passes; and the anus, through which stool passes. Men only have two openings: one at the tip of the penis, the urethra, for both urine and semen; and one behind, the anus, for stool.

The urinary sphincter comprises about one-half the length of the urethra in women. As a muscle, the function of the urinary sphincter is to hold urine in the bladder while the bladder is filling without letting a drop come out. During voluntary urination, the urinary sphincter opens and lets the urine pass out into the toilet. It clamps shut when the bladder is empty in order to allow for bladder filling to resume. It is always contracted and closed, except for the few seconds each day that it relaxes in order for the bladder to empty.

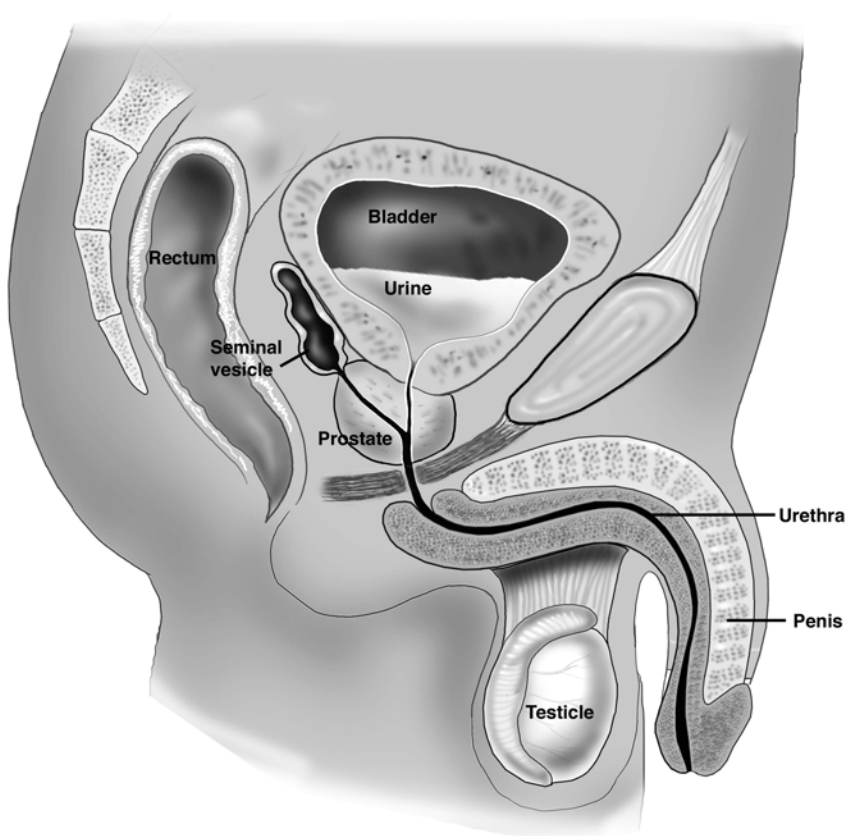


FIGURE 3. *Normal Anatomy of the Male Pelvis.*

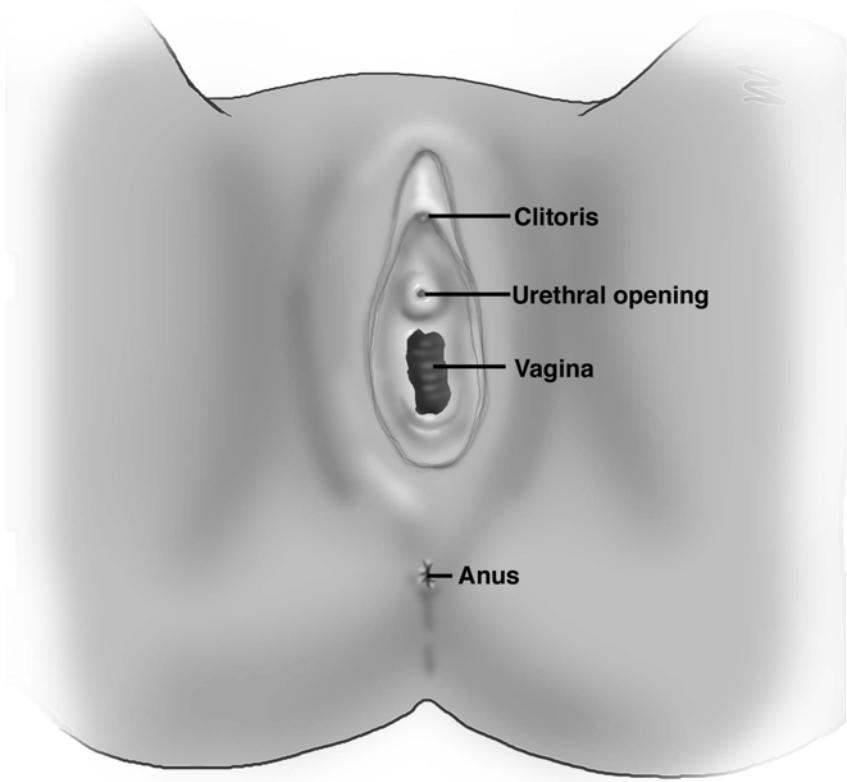


FIGURE 4. *View of the Perineum.*

On a microscopic level (see Figure 5), the fibers that make up the urinary sphincter are organized in a circle. The circle is even, so that when it is contracted, the walls on each side come together and act as a closed, watertight seal, preventing leakage of fluid. Only the urinary sphincter, this wonderful muscle, maintains dryness in the female urinary tract. Damage to the sphincter will result in leakage.

In summary, the female urinary tract comprises four main organs: the kidneys, the ureters, the bladder, and the urethra. But no discussion of the urological conditions in the woman would be complete without reviewing the location of the genital organs in relation to the urinary tract, since these structures play a vital role in urinary health as well (see Figure 6).

The vagina is a muscular canal that sits between the urethra and the anus. The uterus is connected to the vagina through the cervix, which is the passage through which menstrual blood, and, during vaginal delivery, a baby, can pass out of the uterus, into the vagina, and finally out of the body. The uterus is held in place with flexible ligaments that can expand and contract with its changing size due to pregnancy. As the uterus enlarges, the ligaments stretch, and sometimes they become loose. The uterus can lose its supportive tissues and slide into the vaginal canal.

If you are looking from the outside into the pelvis, the bladder sits on top of the uterus. First, you have the pubic bone, then the bladder, and finally the uterus. The two structures, the bladder and the uterus, are separated by a tiny layer of tissue. Their proximity to one another means that they can affect each other. They share some of the same blood and nerve supply. Any of us who experiences frequency of urination and bloating during menstruation knows how much these two organs interact on one another.

The fallopian tubes, which bring the egg from the ovary into the uterus, are connected to and are a part of the uterus. On the other hand, the ovaries are not part of any other organs. They are distinct structures that sit inside the abdominal cavity, which the bladder, the uterus, and the fallopian tubes do not. In order to access the ovaries, the abdomen, which contains the intestines, has to be opened. In addition, the ovaries have a different blood and nerve supply than the uterus and the bladder. The ovaries cannot collapse into the vaginal canal the way the uterus and the bladder can.

If the uterus is removed, the space where the uterus was is filled with loops of the small intestine. No space remains vacant in the human body when an organ is removed. The endless tubes of intestine will find their way into the pelvis, sitting on the top of the vagina. This is important in understanding why some of these organs can wind up in funny places in our bodies.

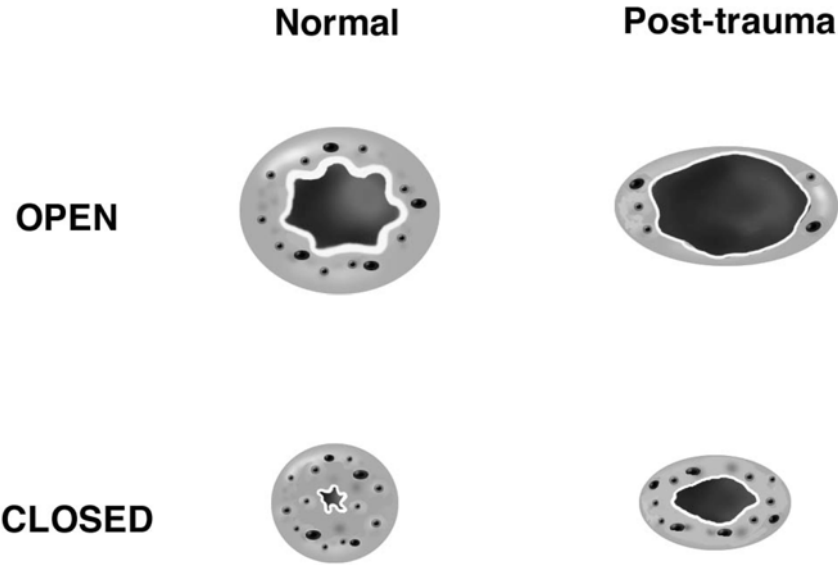


FIGURE 5. *Normal and Post-Traumatic Urethra.*

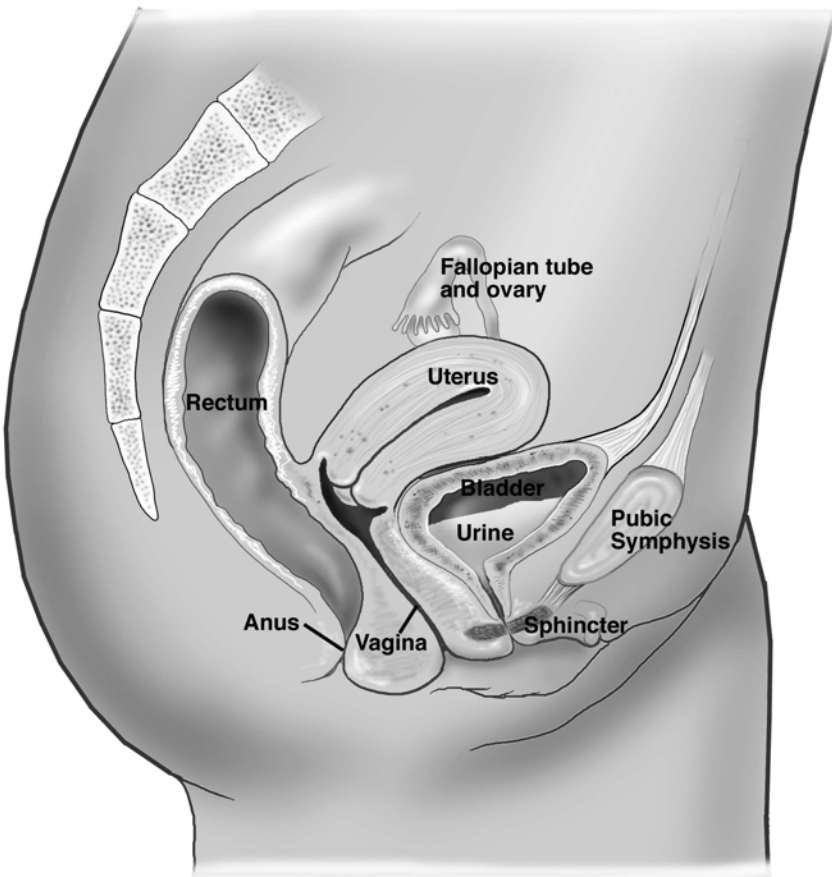


FIGURE 6. *Normal Female Anatomy: Side View.*

Sitting under the vaginal canal is the rectum. If the back wall of the vagina is weak, the rectum can bulge, causing constipation.

To review the anatomy, the vaginal canal is surrounded by three structures: the bladder on the top, the uterus at the end, and the rectum underneath. If you have had a hysterectomy, the uterus is not longer at the end of the vagina; small intestine has moved into its place.

SUMMARY

This discussion lays the foundation for understanding the causes and treatments of the conditions that are discussed later in the book. The four organs of the urinary tract and the uterus and rectum are the main structures that we are discussing. The interaction of these organs with one another will help you to get a sense of what problems we can be faced with and why the symptoms present as they do.

What Can Go Wrong?

Pelvic-Floor Problems: Symptoms and Solutions

I recently had a woman come into the office who was having problems with her bladder since the delivery of her last child. When M.R. was in her thirties and forties, she did not find the problem too bothersome. Mostly, she would have to go to the bathroom frequently, and she couldn't hold it very well when she had the urge to go. Occasionally, she would leak a tiny bit when she laughed hard. Nothing too drastic; she could manage it. Then came menopause and things began to get out of control.

Instead of the occasional accident, M.R. began to have accidents on a regular basis. She would cough and squirt. She would sneeze and squirt. She would get up from a chair and squirt. Sometimes, she would laugh, and not squirt; she would actually pee in her pants! She really didn't have to laugh that hard.

She brought it up with her gynecologist on her yearly examination. He referred her to me. When I examined her lying down, I asked her to cough and she leaked. I noted that her bladder was falling slightly into her vagina, which she could feel at times, although she didn't realize that it was her bladder that was falling down. With a mirror, I pointed out the anatomy so that she could see the problem and understand the proposed treatment.

M.R. had surgery to repair the leakage and the bladder descent. Done vaginally under general anesthesia, the surgery took about an hour to complete. When it was over, she awakened in the operating room, and was transferred to the recovery room with a catheter coming out of her bladder and a packing in her vagina.

The following morning, the catheter and the packing were removed, and she was able to get out of bed and move around. She urinated without difficulty and was discharged home. She felt wonderful that the leakage had resolved completely. She doesn't wear pads anymore, she can

hold her urine longer than she could before the surgery, and she does not get up at night to urinate.

She is pleased with the outcome, and only wishes that she had known that this problem could be solved sooner.

M.R.'s story is typical of women with urinary problems. She had lived with her problem for years before discussing it with a medical professional. Once she brought it up, however, she was directed to a source that could help her, and she was treated effectively. The conditions that are discussed in this book are more common than diabetes, heart disease, and high cholesterol, yet most of us don't know where to turn for help. Many of you don't know what is considered "normal" bladder behavior for someone in your age group, or you have been too embarrassed to ask your physician or even your friends. Therefore, we tend not to report on many of the symptoms discussed in this chapter because we don't realize that these symptoms can be treated or cured.

This chapter is set up to help you "diagnose" your condition in order to learn about the problem from which you are suffering. It is divided into three main categories: painful problems, causes of urinary leakage or incontinence, and symptoms due to pelvic organ prolapse. If you look through the chapter and find the list of symptoms that you have, you can give the condition a name and skip to that chapter directly. In some cases, the presenting complaints are not so straightforward, or perhaps a few different problems are occurring at the same time. A quick overview of all of the urinary tract disorders discussed in the book may also help those of you who are in this category.

CATEGORIES OF UROLOGIC CONDITIONS

- Painful Bladder Conditions
 - Urinary Incontinence
 - Pelvic Floor Prolapse
-

CAUSES OF PAIN

PAINFUL UROLOGICAL PROBLEMS

Urinary Tract Infections
Pelvic Floor Spasms

PAINFUL UROLOGICAL PROBLEMS—continued

Interstitial Cystitis
Radiation Cystitis
Non-bacterial Cystitis
Autoimmune Cystitis
Gynecological causes
Endometriosis
Uterine Fibroids
Ovarian Cysts
Pelvic Inflammatory Disease

Pain is one of the most difficult problems for both patients and doctors to manage. For patients, the frustration of not being understood or taken seriously is unmatched by any other complaint. In many cases, the cause of the pain is not readily identified by objective, conventional, diagnostic methods, so no “physical” abnormalities can be seen. For this reason, many physicians do not acknowledge the pain, further alienating the patient. Therefore, it is impossible to know if any progress is being made in the treatment, except for the patient’s word. You may continue to feel badly, and the doctor just can’t explain why.

In urology, pelvic pain generally results from urinary tract infections, pelvic-floor spasms, interstitial cystitis, post-radiation effects, or gynecological problems, such as endometriosis, fibroids, ovarian cysts, and pelvic inflammatory disease.

Urinary Tract Infections

URINARY TRACT INFECTIONS

(Also called cystitis or bladder infections)
Pain in the pelvis
Frequent urination
Urgency of urination
Burning with urination
Occasionally, blood in the urine
Cloudy urine
Foul odor in the urine

Over 80 percent of you will experience a urinary tract infection at some time during your lifetime. In many cases sexual activity will be the precipitating

factor, but even if you are not sexually active, you can still get them. The symptoms include burning, frequency of urination, back pain, urgency of urination, bloody urine, and, occasionally, leakage of urine. Not all of the symptoms will occur in all women who get cystitis. A diagnosis is made through a urine test which can be done at a local laboratory or at the doctor's office. Most doctors prefer to collect a urine sample before prescribing antibiotics to be sure that you are really suffering from a urinary tract infection. Usually, antibiotics are given for a week to ten days and the symptoms disappear. Many of you suffer from recurrent infections, which are defined as more than three infections in a year. If this is the case, you may need to see a urologist to be sure that no abnormalities within the urinary tract are causing the problem.

Red flags that we look for to suggest that further testing is needed include the following:

1. Infections that began during childhood, before the onset of sexual activity.
2. Infections that result in fevers over 101.5°F.
3. A personal history of kidney stones.
4. A personal history of urinary tract surgery or abnormalities.

Childhood Urological Infections

Infections that began before the onset of sexual activity suggest that an anatomical defect may be present that predisposes you to infections. Usually, if a child develops a urinary tract infection, her pediatrician will refer her to a pediatric urologist for testing. If you remember getting infections as a child, but you have never seen a urologist (an experience that most children remember), it is worth consulting with one now to check things out. The evaluation is usually simple. A kidney ultrasound (sonogram—same test) is done to evaluate the kidneys. This is a painless, noninvasive test that looks at the structure of the kidney. Kidney stones, masses, tumors, cysts, and the absence of a kidney can be detected by ultrasound. The function of the kidneys cannot be assessed, but as a screening test, the ultrasound is the best place to start.

Fevers with Infections

Infections that result in fevers over 101.5°F indicate that one or both of the kidneys may be infected as well the bladder. Most run-of-the-mill urinary tract infections do not migrate up the urinary tract and settle into the kidneys. Even though women with cystitis often suffer from low back pain,

the infection remains contained within the bladder. The low back pain is secondary to inflammation and spasm of the pelvic-floor muscles on which the infected bladder sits. Kidney infections cause pain in the mid-back and flank, immediately under the ribs. In a healthy young woman who is not immunosuppressed, a kidney infection nearly always results in a fever over 101.5°F. Radiographic imaging and a visit to the urologist are warranted if a urinary tract infection results in a fever.

Kidney Stones

If a woman with a history of kidney stones gets a urinary tract infection, an evaluation should be done to be sure that no new stones have grown that have led to the infection. There is a 50 percent chance that any given person will get another kidney stone if she had one previously. Fortunately, however, the second stone tends to occur 8 to 10 years after the original stone. You can have a stone sitting up in the kidney without feeling it. It is only when they pass out of the kidney and get stuck in the small-caliber ureter that intense pain results. Stones can complicate matters because they are usually infected and because they can block the outflow of urine. If a woman with recurrent urinary tract infections has a stone sitting in the urinary tract, it should be removed in order to reduce the risk of getting more infections and to prevent the excruciating pain that can result from the spontaneous passage of the stone. All kidney stones harbor infection. However, not all stone patients suffer from infections and not all infections in stone patients come from the kidney stone. It is wise to get rid of the stone in case it is the cause of the infection. With the sophisticated, noninvasive techniques that we have available now to remove kidney stones, it is a good idea to remove them if they are found.

Surgery

If you had surgery as child to correct an abnormality of the urinary tract, it is a good idea to see a urologist if you are getting recurrent infections. One or two infections per year are not harmful, but more than that suggests that something may not be right. A urologist will order some radiological studies to evaluate the kidneys. The study that is ordered depends on what abnormality you suffered from originally. Often, these x-rays can be difficult to read if the person reading them is not familiar with the defect and its correction. That is where the urologist comes in. The urologist can tell if an abnormal-looking x-ray is within the normal limits of a corrected problem. Many radiologists are experienced in genitourinary radiology and can read these x-rays quite well, but corroborating information between the

two specialists is helpful. In addition, the urologist can determine whether or not the original problem has recurred, progressed, or remained stable. Treatment can then ensue from there.

Pelvic-Floor Spasms

PELVIC MUSCLE SPASMS

Frequency of urination
Sense of incomplete bladder emptying
Urgency of urination
Getting up at night to urinate
Burning after urination
Crampy discomfort in the pelvis

VERSUS URINARY TRACT INFECTIONS

UTI causes burning with urination
UTI causes foul-smelling urine
Must do urine culture to distinguish diagnosis

Pain secondary to pelvic-floor spasms is a common occurrence that many of you will experience at some time during your lifetime. It frequently goes unrecognized by both physicians and patients. The pelvis is a bony structure whose floor is covered in slings of muscle. This muscular floor prevents the pelvic organs from falling onto the ground, just like the abdominal wall muscle holds the intestines inside the body. The bladder, uterus, and rectum sit on the pelvic-floor muscles. Three structures pass through these muscles. They are the urethra (which drains the bladder), the vagina (which is attached to the uterus), and the anal canal.

Just like other muscles in the body, the pelvic-floor muscles can go into spasm. Muscle spasms occur when a muscle contracts without conscious control. The most familiar spasms occur in the lower back. For those of you who have suffered from low back pain, you know that you can bend over in a certain way and cause an injury that results in a muscle spasm. The first line of treatment is usually bed rest to relax the muscle, combined with anti-inflammatory agents, and occasionally steroid therapy. The pelvic-floor muscles can go into spasm in much the same way. The causative event may be subtle, resulting in irritation of the muscles, which then go into spasm.