MECHANISMS OF UROLOGIC DISEASE

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W. B. SAUNDERS COMPANY

Philadelphia 1953 London

Made in the United States of America
Press of W. B. Saunders Company, Philadelphia

Library of Congress Catalog Card Number: 53-9356

PREFACE

AFTER A LIFETIME spent largely in the teaching and practice of Urology, it has begun to seem to the author of this book that it is time to systematize the body of urologic knowledge. This is needed particularly for beginners and for those physicians who are not urologic specialists, and therefore in no position to supply their own rationalization.

The lack of rationality and of system based thereon in most of the urologic books in wide use today is well shown by the fact that they are practically all organized on an anatomic basis—Diseases of the Kidney, Diseases of the Ureter, etc., although it is now generally known that most of the diseases of the urinary tract are system diseases. A really intimate knowledge of the natural history, clinical course and proper treatment of them depends upon one's knowledge of the physiologic processes and pathologic changes involved, much more than on a knowledge of the anatomic arrangements. Urology concerns itself very greatly with disturbances of the conductive function of the urinary tract, and very little with pathologic changes in the renal parenchyma, except as such changes are secondary to obstruction and infection. It is largely on this account that the title "Mechanisms of Urologic Disease" has been chosen.

Keeping these considerations in mind, this book is organized on the basis of eight different types of pathologic changes, as shown in the Introduction, dealing with each as it applies to the entire urogenital tract. This causes certain parts of the text to appear quite unorthodox, particularly those concerned with hydronephrosis, pyelonephritis, contracture of the vesical orifice and "chronic prostatitis." Everywhere an effort has been made to avoid traditional clichés which are unsupported by actual evidence. The author feels strongly that the abandonment of these clichés, and

the substitution for them of valid concepts of disease processes has brought about a dramatic and highly gratifying improvement in the results of clinical treatment. A particularly good example of this is the treatment of chronic or recurrent urinary tract infection (pyelonephritis), which may in time alter markedly our ideas concerning diseases affecting the renal parenchyma. Another is that of "chronic prostatitis," a mere pathologic term, exalted fallaciously for many decades into a disease per se, but now known to be a local change secondary to other lesions, and disappearing when they are corrected.

The book began as a series of introductory lectures to third year students at Jefferson Medical College. Later these lectures were combined into a syllabus for the use of the students and now the syllabus, expanded and modified, makes up the present work. The embryonic form of the arrangement by pathologic entities may be found in "Practice of Urology," published in 1926, and in the writing of which the present author collaborated with Dr. Hugh H. Young. For entirely practical reasons chapters on male infertility, on lesions of the external genitalia, on lesions of the scrotal contents, and on the theory and practice of catheterization have been added, as well as an outline for history taking and physical examination. There are a few charts, but in general illustrations have been judged inappropiate. They may be found in abundance in more extensive works on Urology, and need not be repeated here, where concern is with underlying principles, not with details.

An effort has been made to supply adequate and up-to-date references to the literature, as well as a list of standard works of reference. Urology is a subject in which there is enough variety of opinion so that no one textbook should be used exclusively. As for this book, it has been condensed to the extent of my ability, so that every word is intended to be significant, and should be read as such.

Acknowledgement is made to Dr. George H. Strong for his expert assistance with the chapters on Congenital Malformations and on Neurogenic Bladder.

DAVID M. DAVIS

June, 1953

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Introduction

A PROPER CONCEPT of urologic disease as seen in the patient can be had only through a thorough knowledge of the pathologic changes underlying it. There are eight types of pathologic change, one or more of which is present in practically every case of urologic disease. Urology is here presented on the basis of these eight types of pathologic change. By noting the presence or absence of each in an individual case, the case can be analyzed into its essential parts, and the proper therapeutic measure or measures logically and intelligently planned.

The eight types are as follows:

1. Obstruction
2. Infection
3. Stone formation (calculosis or lithiasis)
4. Neoplasm
5. Congenital malformation (anomaly)
6. Trauma (mechanical, chemical, thermic, electrical or radiation injury)
7. Foreign body
8. Neurogenic (changes consequent on disease or injury of the nervous system)

These changes are often mutually interdependent; for example, (1) obstruction (that is, the partial or complete stasis of urine resulting from obstruction) predisposes to infection, and makes infection, once established, persistent; (2) neoplasm, congenital malformation, trauma, stone formation, or chronic infection may cause or increase obstruction; (3) obstruction and/or infection may predispose to stone formation; (4) foreign body predisposes to infection; (5) neurogenic changes, by lessening the expulsive power of the muscles surrounding the urinary tract, may produce

stasis of urine, and so predispose to infection just as obstruction does.[1]

The eight types of pathologic change will be taken up seriatim.

[1]Hinman, Frank B.: The Principles and Practice of Urology. Philadelphia, W. B. Saunders Co., 1935.

Obstruction

To comprehend the effects of obstruction on the urinary tract, its normal function must be thoroughly understood.

Urine is secreted by the glomeruli and convoluted tubules, which make up the parenchyma of the kidney. It is forced along the convoluted tubules, and eventually the collecting tubules, by the secretory pressure of the additional urine being secreted behind it. The potential secretory pressure of the kidney approximates closely the capillary pressure, namely, about 60 mm. of mercury in a person with normal arterial pressure. The pressure necessary to move the urine along the tubules under normal circumstances is probably very low. If anything impedes this flow so that the pressure rises to a point approximating the secretory pressure, all secretion stops. If, however, the pressure in the tubules rises to any considerable degree, even though it remains below secretory pressure, the secretion of urine is hindered and made inadequate.

This fact indicates a fertile field for further investigation. To evaluate properly all studies, whether experimental or clinical, of abnormal renal function, the intrapelvic pressure should be known. The obvious difficulties of determining intrapelvic pressures have prevented such studies in the past, but in the future means of so doing must be devised. The mechanical conditions governing the circulation of the blood have been, and are being, studied in the most thorough manner. These studies have given birth to the science of *hemodynamics*. There is every reason why equally careful study should be made of the mechanical arrangements and pressure conditions of the urinary tract. It is to be hoped that internists and physiologists generally may become aware of how

greatly the well-being of the renal parenchyma depends upon the preservation of normal pressure in the renal pelvis. We shall then have a full-blown science of *urodynomics*.

The problem is complicated by the fact that elevated intrapelvic pressure is often complicated by infection. There is sufficient evidence to show that kidneys damaged by elevated intrapelvic pressure with or without infection may become unable to excrete adequately nonprotein nitrogenous substances (urea, creatinine, etc.), thus leading to azotemia, and at the same time they may be unable to retain sodium, potassium and chlorides so that they are excreted excessively, leading to deficiencies of any or all of these substances in the blood and tissues. It is also true that while one of these crystalline substances may be excreted in excess, another may be retained. This is a very important addition to our knowledge, since hypokalemia, hypochloremia or hyperchloremic acidosis may prove fatal just as well as uremia.[1]

The importance of maintaining a low intrapelvic pressure is such that the mechanism of the calyces and pelvis of the kidney, and of the ureter, is designed to remove from the kidney all urine as rapidly as it is formed, and keep the pressure at the outer ends of the collecting tubules (on the pyramids) at a very low point, normally not more than that of a column of water about 5 or 10 cm. high.[2]

From the tip of the pyramids onward, the whole function of the remainder of the urinary tract is (1) to conduct the urine to the exterior and (2) to store it in the bladder so that its discharge may be at intervals instead of continuous. (This intermittent discharge

[1]Symposium on Normal and Abnormal Renal Function: Berliner, R. M., et al., Earle, D. P., et al., Pines, K. L. and Mudge, G. H., Am. J. Med., *11:* 274-311, 1951; Danowski, T. S.: Newer Concepts of the Role of Sodium in Disease. Am. J. Med., *10:* 468, 1951; Martin, H. E., et al.: Etiology and Treatment of Serum Potassium Defects. J.A.M.A. *147:* 24, 1951.

[2]Personal observations on patients with nephrostomy tubes and apparently normal ureteral function. This assumption was based on the following: (*a*) After the removal of the nephrostomy tube, there were no pain, no fever, and no urinary drainage; (*b*) in a short time the urine was sterile, and the function of the kidney in question was normal; and (*c*) at a later date the urogram was normal.

of urine is a necessity of terrestrial life; fish have no urinary bladders because they do not need them.)

The kidney pelvis and calyces are surrounded by a thin layer of smooth muscle. In the calyces and infundibula, this is said to produce a "milking" or sort of peristaltic movement.[3] The muscle of the pelvis proper contracts whenever enough urine collects in it to raise the pressure ever so slightly, probably only that of a few centimeters of water. Narath states that at this moment the "calyceal sphincter" closes, preventing reflux into the collecting tubules. This forces urine into the upper portion of the ureter, which in turn contracts, forcing the urine further down.[4] This ureteral muscular contraction then continues down the ureter as a peristaltic wave, forcing the portion of urine ahead of it, and taking one to three seconds to reach the bladder. The contraction wave is strong enough to close the lumen of the ureter completely, so that no urine can leak back into the pelvis. The segment of ureter below the contraction wave is relaxed, so that the progress of the urine is unimpeded. After the wave has passed, the muscle relaxes, but the ureter remains collapsed and empty until the next peristaltic wave comes along. This mechanism keeps the kidney pelvis practically empty at all times, and explains (1) why urine passes continually from the kidney to the bladder, regardless of the position of the body (consider the bat, which hangs upside down most of the time) and (2) why the outline of the complete ureter is never seen in intravenous urograms of normal ureters.[5]

At the lower end of the ureter, the muscles surrounding it are thicker and stronger than at the upper end, and are able to drive the urine into the bladder against any pressure that ever exists in the normal relaxed bladder. With a cystoscope, these intermittent jets of urine can be seen spurting into the bladder. If the secretion of urine becomes more rapid, the ureteral muscles do not contract

[3]Narath, Peter A.: Renal Pelvis and Ureter. New York, Grune and Stratton, 1951.

[4]Caulk, J. R., and Gruber, C. M.: Surgery of the Ureter. Nelson's Loose-leaf Living Surgery, Vol. VI, Urology. New York, Thos. Nelson and Sons, 1941, p. 693.

[5]Lapides, J.: The Physiology of the Intact Human Ureter. J. Urol. *59:* 501-537, 1948.

more strongly nor more rapidly, but the peristaltic waves become more frequent, so that very large amounts can be transported in a short time. It is interesting that this peristaltic wave mechanism operates through the intrinsic unsheathed nerves and ganglia of the ureter, and continues even if the ureter is entirely separated from the rest of the nervous system.

The bladder is surrounded by a layer of smooth muscle, much thicker and stronger than that of the ureter, and capable of producing a much higher pressure. This muscle occurs in interlacing bundles running in all directions. It is called the detrusor muscle of the bladder, as it supplies the force which expels the urine from the bladder. Certain of these bundles separate from the others and swing about the vesical orifice in a loop, called the internal sphincter or internal arcuate muscle of the bladder.[6] These muscles are innervated from the autonomic nervous system (both sympathetic and parasympathetic). Control is exercised by reflex centers in the cauda equina in such a manner that, while the bladder is filling, the detrusor is relaxed and the internal sphincter either contracted or maintained in a rather high state of tonus. This retains the urine in the bladder. When the bladder is full, a desire to void is felt, and the voiding reflex is set off by voluntary impulses from the cerebrum. In this reflex the internal sphincter relaxes (or is pulled open), and the detrusor muscle contracts, thus forcing the urine out of the bladder. The urine can be controlled for a time by voluntary contraction of the external sphincter, which is composed of striated (voluntary) muscle and innervated by sheathed fibres from the pudendal (pudic) nerve. If, however, the bladder becomes very full, the sensory impulses become so strong that the voiding reflex is set off, and voiding occurs in spite of the greatest efforts to inhibit it. The normal detrusor muscle is able to raise a column of water to a height of about 6 feet.[7]

Except for the sphincters, there is no muscle about the urethra,

[6]Wesson, M. B.: Anatomical, Embryological and Physiological Studies of the Trigone and Neck of the Bladder. J. Urol., *4:* 279-15, 1920.

[7]Langworthy, O. R., Kolb, L. C. and Lewis, L. G.: The Physiology of Micturition. Baltimore, Williams and Wilkins, 1940; also Muellner, S. R.: The Physiology of Micturition. Bull. New England M. Center, *12:* 93, 1950.

and the last drops of urine must be expelled by shaking the urethra or by pressing upon it, or else be allowed to drip out by gravity.

Generally speaking, the strength of the sensory impulses giving a desire to void is proportional to the pressure within the bladder. Psychic influences may affect this. The thought of voiding, fear, or the sound of running water may cause partial contraction of the detrusor, bringing about an increased desire to void. If, on the other hand, the mind is strongly diverted to other matters, the detrusor may remain relaxed until the bladder contains an unusually large amount of urine.[8] The action of the bladder muscles can be studied by a new method, electromyography, which may provide important information and better diagnostic means in the future.[9]

The varying size and strength of the muscles in different parts of the urinary tract is important for the following reasons: If the pelvis or upper ureter is torn, urine escapes into the tissues under very low pressure, and does comparatively little harm. If, however, the bladder or urethra is torn, urine is forced into the tissues by the strong contractions of the detrusor muscle of the bladder so that it extravasates to great distances, with serious and often fatal consequences.

FUNCTIONAL DISTURBANCES CAUSED BY OBSTRUCTION

Obstruction may be caused by anything which diminishes the caliber of any tubular part of the urinary tract (infundibulum, ureter, urethra), either by pressure from the outside, or by a constriction resulting from some abnormality in the wall of the tubular structure. Such abnormality may be acquired, for example, a stricture (inflammatory, traumatic, neoplastic); or congenital, for example, a narrowing at any point due to improper development.[10]

An obstruction at any point can have no direct effect on any

[8]Evans, C. L. E.: Starling's Principles of Human Physiology. 11th ed. Philadelphia, Lea & Febiger, 1952, Section on the Physiology of Micturition, 1025-1035.

[9]Boyce, W. H.: Bladder Electromyography: A New Approach to the Diagnosis of Urinary Bladder Dysfunction. J. Urol., *67:* 650, 1952.

[10]Ostling, K.: The Genesis of Hydronephrosis. Acta Chir. Scand., *86:* Suppl. 72, 1942.

part of the urinary tract *below* that point, but it does have a direct effect on every part of the urinary tract *above* the point of obstruction. What are these effects, and how are they brought about?

The diameter of the normal ureter in the adult is roughly 4 mm., and of the urethra roughly 9 mm. If the diameter of either is reduced by even a little, it is easy to see that it will take longer for the same amount of urine under the same pressure to pass the obstructed point. Whenever this occurs, the muscles above the obstruction react by contracting more strongly, thus increasing the pressure above the obstruction to a point above normal. This causes the urine to pass the obstructed area at a greater *velocity,* and therefore in the same *time* as before. This reaction *compensates* for the obstruction, and may cause pain or other abnormal sensations, but often causes no abnormal sensation, so that the patient is entirely unaware of it. As the muscles continue to contract more strongly than normally, they undergo hypertrophy, like the muscles of an athlete in training. This state of compensation might go on forever, except that obstructions tend to become more severe, slowly or rapidly, as time goes on. Eventually, even the hypertrophied muscle is unable to expel all the urine present before it becomes fatigued. Its battle against obstruction then becomes a losing one. If in the ureter, the ureter above the obstruction never becomes quite empty, and the peristaltic waves are thereby rendered ineffective. If this situation develops fairly rapidly, the muscles make strong and spasmodic efforts to expel the urine, causing severe pain (colic, ureteral or renal). If it develops slowly as, for example, in the case of congenital obstruction, there may never be any pain whatever, or there may be constant, dull and aching pain, or there may be only symptoms referred to other organs.[11]

With the stagnation of urine in the ureter, the pelvic pressure

[11]Some greatly dilated ureters have been thought to be due to deficient nerve supply, and have been called megaloureter (like megacolon). Recent studies suggest that the dilatation may really be obstructive, and the obstruction a congenital stenosis or a short paralyzed segment of the lower ureter. See Campbell, E. W.: Megaloureter. J. Urol., *60:* 31, 1948; and Swenson, O., MacMahon, E., Jacques, W. E. and Campbell, J. S.: a New Concept of the Pathology of Megaloureter. Bull. New England M. Center, *13:* 157, 1951.

is bound to rise, whereupon the renal function will be impaired. If the obstruction is located in the lower part of the ureter, the intrapelvic pressure will not rise until the ureter is decompensated, but if the obstruction is in the upper part of the ureter, or at the ureteropelvic junction, the pelvis is immediately affected. Long continued severe obstruction produces hydronephrosis and hydronephrotic atrophy, as explained in a subsequent paragraph, but lesser degrees of obstruction have important effects, even when the kidney pelvis is not greatly, or even very little, dilated. These effects are very difficult to study accurately, and are not as yet fully investigated and understood (*vide supra*). At present, however, we may say that at least three types of clinical changes occur: (1) persistent pain in the kidney region, (2) persistent or recurring infections in the affected kidney, and (3) referred symptoms, especially anorexia, nausea, vomiting, and abdominal pain. One, two or all of these may be present in an individual case. In addition, there is excellent reason to believe that obstructions affecting the kidney may cause, or help to cause, stone in the kidney, and that intermittent hematuria may be caused by obstruction. The urinary stasis (stagnation) associated with even minor degrees of obstruction is almost certainly the reason why the regions above the obstruction are more apt to become and to remain infected than the normal. Severe renal damage produced by such chronic infections may be difficult to distinguish, either clinically or under the microscope, from certain diseases thought to be primary in the parenchyma (arteriosclerotic kidney, nephrosclerosis).

Since the urine is normally transported through the ureter by peristalsis, it is interesting to consider how it makes its way through greatly dilated ureters into the bladder. That it does so is evident from the fact that patients with both ureters dilated may pass normal amounts of urine from the bladder each day, and may live on in apparently good health for long periods. Since there is no peristalsis, pressure in the pelvis must be higher than normal, due to the contractile power of the ureteral and pelvic muscles pressing the urine against the obstruction. Since some urine flows out past the obstruction constantly, the only way the high pelvic pressure can be maintained or increased is by the pressure of newly secreted

urine coming from the collecting tubules. This means that the urine must be secreted against a much higher intratubular pressure than normal. In spite of the great quantity of most excellent work done in the past few years, with measurements of blood pressure in the renal arteries and veins, blood flow through the kidney, glomerular filtration and tubular secretion and resorption of all known urinary constituents, we still remain in ignorance of the effect on all these matters of the increased intrapelvic and intratubular pressure consequent on obstruction, whether it be slight or severe, recent or of long standing.[12] This is a most fertile field for future research on kidney function.

If the obstruction is below the bladder, the detrusor muscle reacts in the same way as that described for the ureteral muscle, with hypertrophy and stronger contractions. It also becomes more irritable, so that the bladder will hold less urine, and the call to urinate may be very strong (*urgency*). Severe urgency may cause enuresis in children, and must be carefully distinguished from psychic enuresis. (The author is of the opinion that 10 or 15 per cent of all cases of enuresis are on a physical basis of obstruction or neurogenic bladder.) The distinction can be made by uroflometry and cystourethroscopy. The increased irritability results in more frequent voiding (*frequency*), but no sense of difficulty. At first compensation is perfect, and the voiding stream is unchanged. Later it becomes weaker and the patient may be conscious of *difficulty* in urinating, and try to accelerate the flow by *straining* or *forcing* with the abdominal muscles. *Burning* pain may occur. Eventually the stream becomes so slow that the detrusor muscles tire before the bladder is empty. They may try again, in a moment or two, after recovering their strength. This brings about what is called *interruption,* or *multiple voiding* (double, triple, and so on). If, in spite of repeated efforts, the bladder cannot be completely emptied, the urine left in it is called *residual urine,* and *decompensation* of the bladder has begun (like decompensation of the heart).

[12]Smith, H. W.: The Kidney: Structure and Function in Health and Disease. New York, Oxford University Press, 1951; Pitts, R. F.: Modern Concepts of Acid-Base Regulation. Arch. Int. Med., *89:* 864, 1952; Share, L.: Effect of Increased Ureteral Pressure on Renal Function. Am. J. Physiol., *168:* 97, 1952.

Note, however, that unmistakable symptoms and signs of obstruction are present before residual urine develops. As the amount of residual urine increases, the muscle fibres are stretched more and more, until they reach a point where they cannot contract efficiently. The bladder then becomes *dilated* or completely decompensated. Some urine may leak out from time to time, due to increases in abdominal pressure, or to fugitive contractions of the dilated muscle (*paradoxical incontinence*). In general, however, the pressure in the dilated bladder is just that provided by the thrust of the ureters propelling urine into it. It is therefore a *constant* pressure, with no periods of relaxation as in the normal. It thus becomes more and more difficult for the ureters to discharge urine into the bladder, and when the bladder pressure reaches the maximum that can be produced by the ureteral muscles, they can no longer do so.[13] The urine remains in the ureters, the ureters become dilated, the pressure in the renal pelvis becomes increased, and all the evil effects of obstruction on the kidney begin to occur. This can be described as decompensation of the ureters.

While compensation is perfect, obstruction may not be suspected unless there are painful sensations. Even in this stage, however, infection may be favored and kept up, so that the mere existence of chronic or recurrent infection may be put down as strong evidence pointing to obstruction even in the absence of other symptoms. Later, however, the stream becomes slower and weaker, and this slowing may be evident if one simply observes the patient while voiding. If there is doubt, a *uroflometric* test may be done.[14] The uroflometer is a simple instrument which measures the rate of flow of the urinary stream. In the adult the normal rate should be not less than 22 cc. per second. If it is less than this, either (*a*) the detrusor muscle is weakened, causing abnormally low bladder pressure, or (*b*) the urethra is narrowed at some point; that is, there is an obstruction. The bladder pressure can be determined by a cystometric test (see the section on Neurogenic Bladder). Thus if one determines that the bladder pressure is normal or

[13]Henderson, V. E.: The Factors of Ureter Pressure. J. Physiol., *33:* 175-188, 1905-06.

[14]Drake, W. M., Jr.: The Uroflometer: An Aid to Study of the Lower Urinary Tract. J. Urol., *59:* 650, 1948.