Avicenna, the Iranian scientist, describes the mechanisms of normal voiding in his famous book, *the Canon of Medicine*. Then, he enumerates urinary symptoms. In this article, his discussion on dysuria, its causes, and its pathophysiology is compared with these concepts in modern urology. Avicenna points to some etiologic theories of interstitial cystitis and chronic prostatitis. In *the Canon*, we can distinguish bases of the theory of infection and mucosal theory, along with abnormalities of urine, psychological factors, and abnormalities in prostatic secretions. Avicenna also indicates some differential diagnoses of and associated disorders with interstitial cystitis. His short but rather concise discussion on oliguria and its causes is an interesting point for urologists and nephrologists.

**INTRODUCTION**

In the previous three parts of these articles, I reviewed chapters of the *Canon of Medicine*, written by Avicenna—the Iranian scientist in the 10th century—on the bladder and its diseases with modern urological findings. In this part of this article series, I continue with the 2nd treatise of book III, part 19, which is on urine, voiding, and urinary symptoms.

**MATERIALS AND METHODS**

This study is the comparison of modern urology with the urological chapters of Avicenna’s *Canon of Medicine*. I used *the Canon* in its original language (Arabic), along with its Persian translation. The 2nd treatise of part 19 of book III covers normal voiding and its mechanisms, as well as urinary symptoms. I compared the text with the current urological findings. Selected topics from *the Canon* are presented and a brief discussion follows each subject. I translated the original Arabic version into Persian and compared it with the available Persian translation in order to present an accurate text.

I skipped Avicenna’s discussions on traditional and herbal medicine as these subjects were not comparable with the modern therapeutic methods, and thus, they were beyond the aim of this study. I was only engaged with the items that the current modern medicine obviously and clearly proceeds with them.

**DISCUSSION**

**Book III, Part 19, Treatise 2**

Part 19 of book III in the *Canon* is entitled “On Urinary Bladder and Urine.” This part has 2 treatises: treatise 1 is on the urinary bladder...
and treatise 2, on urine and its timing. In the three previous articles of this series, I analyzed in detail the 1st treatise which included filling or reservoir function of the urinary bladder and its abnormalities such as disability and laxity of the bladder and various inflammation disorders of the bladder. In treatise 2, Avicenna discusses the emptying or voiding function of the urinary bladder and its abnormalities.

**Book III, Part 19, Treatise 2, Chapter 1**

*When urine accumulates in the bladder and it needs to be emptied, the bladder contracts from every side, and at the same time, the muscle of the bladder outlet [famol masaneh in Arabic] opens. And in this way, urine goes through the path of exit by the aid of the pressure of the muscles of the soft part of the belly [meragh in Arabic].*

**Discussion.** In chapter 1, “on mechanism of normal voiding,” Avicenna describes in brief the bladder emptying and voiding. Of interest, he describes carefully the contraction phase of bladder function and inhibition of bladder neck guarding mechanism during voiding. He also explains carefully the synergism between bladder contraction and its neck’s inhibition during voiding. These are completely in line with the modern urophysiology.

**Book III, Part 19, Treatise 2, Chapter 2**

*The symptoms that originate from abnormal status of urine are: (1) dysuria, (2) difficult voiding, (3) urinary retention, (4) frequency, (5) dribbling, and (6) abnormally excess urine in disorders including diabetes [Diabitos in Arabic].*

**Discussion.** Avicenna here enumerates some lower urinary tract symptoms that include symptoms of bladder outlet obstruction.

**Book III, Part 19, Treatise 2, Chapter 3**

*Dysuria [hergatal bel in Arabic] is induced by the following situations: (1) urinary matter is pungent and borax [alkaline; bouraghi in Arabia] due to abnormal temperament; (2) there is a matter which is necessary for regulation and preparation of the urinary substance. When it is absent, the result is dysuria. This necessary substance for regulation of urinary temperament is a moisturizing material in fleshy gland [prostate] that is nutritious and rich. This moisturizing material is flowing through the urethra and sticks to it and covers it. When this substance is removed, the urinary pathway is left without this sticky cover, and also, the lubricant material is urine is removed. Thus, its regulatory and preparatory function is stopped.*

**Why is this moisturizing substance with its useful function removed? It has 2 causes. First, sexual intercourse is responsible. This moisturizing substance often exits in large amount along with seminal fluid. Thus, it is not surprising that if a person has frequent sexual intercourses, he will have dysuria, too. Second, the cause is body melting [cachectic] diseases that causes removing this moisturizing material. Third, there is possibility of desquamation or pustules [jarab in Arabic] or ulcer in the penile urethra that causes disuria.**

If urine is pungent and borax [alkaline], its only sign is urinary pungency [acuity], and there is no pus in urine. However, if dysuria is due to pustules or ulcer in the penile urethra, its sign is discharge of pus or dirt with urine. It is frequent that the pungent urine causes pustules or ulcer in the bladder. Thus, pungent urine is a predisposing factor for developing pustules or ulcer in the penile urethra, so as biliary diarrhea is a predisposing factor for intestinal ulcer.

If dysuria is associated with pus and blood, its management is the same as the management of bladder ulcer. However, if it is not due to ulcer and there is no pus in urine, its best management is cleansing the urine [by herbs] and that you make the urine to be drained. Avoid pungent, salty, and very sweet diets. The patient must not make himself tired and must not have sexual intercourse. If the cause of dysuria is the dry state of the glands, you should do something for recovery of normal moistures of the body and you should avoid any thing that dries your body such as sexual intercourse.
**bladder syndrome/interstitial cystitis (PBS/IC)** and prostatitis or prostatitis-like syndrome. Painful bladder syndrome/interstitial cystitis is a condition diagnosed as a clinical basis today requiring a high index of suspicion by the clinician. It is likely to have multifactorial etiology that may act predominately through one or more pathogens resulting in the typical symptom complex mostly in women (female-male ratio, 5:1). In modern urology, the proposed causes of PBS/IC are infection autoimmunity and inflammation, mast cell involvement, bladder glycosaminoglycan and epithelial layers permeability, neurobiologic factors, anti proliferative factor, urine abnormalities, and other potential factors such as anxiety, psychological stresses, mood dysregulation, and pelvic floor dysfunction. The counterpart entities in men is prostatitis and prostatitis-like syndromes that are very prevalent, being seen in 2% to 10% of men. Prostatitis is the most common urologic disease in men younger than 50 years old. The etiologies of prostatitis and prostatitis-like syndromes is similar to those of PBS/IC. They include microbiologic causes (gram-negative uropathogens, gram-positive bacteria, anaerobic bacteria, Corynebacteria, Chlamydia, Ureaplasma, nonculturable microorganisms, and fungi), altered prostate health factors, dysfunctional voiding, intraprostatic ductal reflux, immunologic alterations, chemically induced inflammation, neural dysregulation/pelvic floor muscular abnormalities, interstitial cystitis-like causes, and psychological factors.

**Discussion 2.** Avicenna refers in the Canon to some modern theories (infection theory and mucosal theory). The first one is infection, especially sexually transmitted disease. In modern urology, it has been proven that sexually transmitted organisms and some sexual behaviors such as unprotected penetrative anal intercourse can induce prostatitis and dysuria. At that time, Avicenna was not aware of nonspecific and specific pathogens involved in urinary tract infections; consequently, he attributed the symptoms to loss of moisturizing substance of urothelium due to infection. Today in modern urology, this attribution is not completely rejected because of 2 reasons: first, infection has a major role in bacterial prostatitis, but most of the cases are nonbacterial prostatitis and prostatodynia. Second, in interstitial cystitis, urinary tract infection may trigger its symptoms, but it is unlikely in some patients that active infection is involved in the ongoing pathologic process or unlikely that antibiotics have a role to play in treatment.

**Discussion 3.** The mucosal theory or bladder glycosaminoglycan layer theory is one of the most acceptable theories in the pathogenesis of interstitial cystitis. It is based on the absence of “moisturizing substance in urine” theory of Avicenna. He mentions that this moisturizing substance is necessary for regulation and preparation of the urinary matter, and it is nutritious. It is flowing through the urethra and sticks to it, and if removed, its function is stopped and thus dysuria ensues. Parsons and Hurst hypothesized and popularized the concept of “defect in the epithelial permeability barrier of the bladder surface glycosaminoglycans” in inducing PBS/IC. The major classes of glycosaminoglycans are hyaluronic acid, heparine sulfate, heparin sulfate, chondroitin, dermatan sulfate, and keratan sulfate. These carbohydrate chains coupled to protein cores produce diverse classes of macromolecules, the proteoglycans. Glycosaminoglycans exist as a continuous layer on bladder urothelium. Except heparine, all the other types of glycosaminoglycans have been found on the bladder surface. The glycosaminoglycan layer functions as a permeability barrier and anti-adherent. In the absence of this protective layer, the urinary bladder’s susceptibility to infection would increase. Parsons and Hurst reported lower excretion levels of urinary uronic acid and glycosaminoglycans in patients with interstitial cystitis than in healthy volunteers. Support for epithelial abnormality from a different perspective (genetic studies) has come from Bushman and colleagues and further information on an abnormal surface came from Moskowits and colleagues. The glycosaminoglycan concept for interstitial cystitis of course has some opponents, and it is still at theoretical level.

**Discussion 4.** Another theory of interstitial
cystitis to which Avicenna points is urine abnormalities. He describes it as "pungent and borax" urine without indicating pus in urine.\(^{(4,5)}\) Current theories of pathogenesis generally involve access of a component of urine to the interstices of the bladder wall, resulting in an inflammatory response induced by toxic, allergic, or immunologic means.\(^{(9)}\) This substance acts as initiator only in particularly susceptible individuals or may act like a true toxin, gaining access to the urine by a variety of mechanisms or metabolic pathways.\(^{(21)}\) In Clemmensen and coworker’s study,\(^{(22)}\) the histology suggested a toxic rather than allergic reaction. Circumstantial evidence for the toxicity of urine in interstitial cystitis is suggested by the failures of substitute cystoplasty and continuous diversion in some of these patients because of the development of pain or contraction of bowel segments over time.\(^{(22-26)}\) Also in prostatitis, there is an etiologic theory named “chemically induced inflammation.” Accordingly, urine and its metabolites (eg, urate) are present in prostatic secretion of patients with chronic prostatitis.

**Discussion 5.** Concerning psychological factors in the management of dysuria, Avicenna recommends these patients not make themselves tired and avoid sexual intercourse.\(^{(6)}\) Among the etiologic factors of interstitial cystitis, anxiety, psychological stresses, and mood dysregulation have their own roles,\(^{(8)}\) and psychological factors always have considered to play an important role in exacerbation of chronic prostatitis symptoms.\(^{(9)}\)

**Discussion 6.** Prostatic secretion is scrutinized by Avicenna. He points to the role of a fleshy gland with its nutritious moisturizing substance, the lack of whose secretions induces dysuria.\(^{(4)}\) In part I of this article series, I showed that the gland Avicenna describes is the prostate.\(^{(1)}\) The nutritious secretion that Avicenna described 10 centuries ago are—according to the modern urophysiology—nonpeptide components such as citric acid; polyamines including spermine; phosphorylcholine; cholesterol; lipids; zinc; and secretory proteins such as prostate-specific antigen, human kallikreins, prostate-specific transglutaminase, semenogelin, beta-microseminoprotein, beta-inhibin, leucine aminopeptidase, lactate dehydrogenase, immunoglobulins, complement 3, and transferrin.\(^{(27)}\) First, the relation between prostatitis and citric acid has been investigated.\(^{(28)}\) Second, it is possible that polyamines and their aldehyde products, which produce the characteristic odor of semen, protect the urogenital tract from infectious agents.\(^{(25)}\) Third, high levels of zinc in human seminal plasma appear to originate principally from secretions of the prostate.\(^{(29)}\) An important role of zinc in prostatic secretion has been postulated in a study of Fair and coworkers,\(^{(30)}\) which suggested the dominate role of zinc as a prostatic antibacterial factor. In the study of 36 men free from bacterial prostatic infection, the mean value of zinc in prostatic secretions was 350 mg/mL (range, 150 mg/mL to 1000 mg/mL), while in patients with documented chronic bacterial prostatitis, a reduction of more than 80% to an average of 50 mg/mL (range, 0 to 139 mg/mL) in zinc concentrations. In vitro studies of free zinc ions at concentrations normally found in prostatic fluid have confirmed the bactericidal activity of zinc against a variety of gram-positive and gram-negative bacteria; however, a considerable part of zinc in the prostate appears to be bound to unique proteins such as metallothionein, and this might alter the biologic properties of zinc.\(^{(31)}\) Fourth, there are immunoglobulins in human seminal plasma and they are found in expressed prostatic fluids, which may be related to infections.\(^{(32,33)}\) And fifth, chronic prostatitis also has been shown to be related to complement 3 concentration.\(^{(34)}\)

**Discussion 7.** Avicenna mentions some conditions in the bladder that today are included in the differential diagnosis of interstitial cystitis, such as bladder tumors or desquamation and “body melting” disease.\(^{(4)}\) Diagnosis of interstitial cystitis is made after ruling out the other causes of lower urinary tract symptoms such as urinary tract infection, bladder tumors (especially carcinoma in situ), bladder calculi, tuberculosis cystitis, and radiation cystitis.\(^{(8)}\) Disability and voiding problems in cachectic states (called “body melting” in the Canon) lead to chronic urinary infection, urinary retention, hospitalization, and catheterization which induces dysuria.
Discussion 8. An interesting point is this part of the Canon is attention of Avicenna to the similarity between some bowel disorders and dysuria induced by interstitial cystitis that is on the agenda today in modern urology, too. Avicenna studies the relation of biliary diarrhea with intestinal ulcer. The associated disorders of interstitial cystitis, according to modern texts, are allergies, irritable bowel syndrome, fibromyalgia, systemic lupus erythematosus, inflammatory bowel disorders, vulvitis, and Sjogren syndrome. Thirty percent of patients are diagnosed with irritable bowel syndrome. In these patients, intestinal pain is induced with gas accumulation volumes lower than that which causes pain in healthy persons, similar to the pain of bladder distention in patients with interstitial cystitis. This has been confirmed by Koziol, too. Also, inflammatory bowel disease was found in more than 7% of a population with interstitial cystitis. Alagiri and colleagues found that in comparison with the general population, patients with interstitial cystitis are 100 times more likely to have inflammatory bowel disease and 30 times more likely to have systemic lupus erythematosus. Abnormal leukocyte activity has been implicated in both interstitial cystitis and systemic lupus erythematosus. The similarity of these to what Avicenna cited 10 centuries ago about differential diagnosis of dysuria, especially his emphasis on the presence or absence of pus in urine, is noteworthy.

Book III, Part 19, Treatise 2, Chapter 4

Oliguria can be due to the below causes: (1) drinking inadequate liquids, (2) body porosity, (3) effect of diarrhea on the body, (4) disability of the kidneys, resulting in impaired absorption of fluids, and (5) disability of the liver in separation of the fluid and sending it to the kidneys, so as in hepatic cirrhosis [son of gonieb in Arabic] and drypys state [estesgha in Arabic]. You should know that sour diets are harmful to the patient, and sexual intercourse aggravates the disease.

Discussion. In this chapter, Avicenna enumerates the causes of oliguria. In modern urology and nephrology, this sign it the cardinal sign of acute renal failure, with the following causes: (1) prerenal renal failure due to dehydration, sepsis, and reduced cardiac output; (2) hepatorenal syndrome; (3) iatrogenic causes including drugs' side effects; (4) vascular disorders; (5) intrarenal (parenchymal) diseases such as nephritis and acute tubular and cortical necrosis; and (6) postrenal causes. Avicenna points to most of these causes. He also recommends avoiding astringent and “sour” (acidic) diets, which reminds us that renal failure causes metabolic acidosis.

REFERENCES