MECHANISMS OF URINARY TRACT INFECTION

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ABSTRACT — Most urinary tract infections begin as a cystitis secondary to decreased host resistance brought on by disruption of tissue integrity or a decrease in blood supply to the bladder. In the female, infrequent voiding and the uninhibited bladder are the most common causes of urinary tract infection and are best treated by healthy voiding regimens; while in the male, structural and functional obstructive uropathy are most often associated with urinary tract infection and are alleviated by lowering the high intravesical pressures via surgical or medical measures. The concept that host resistance is the determinant of infection rather than the organism has permitted the use of clean, intermittent self-catheterization; clean intermittent self-dilatation; and transurethral diverticulectomy in the therapy of a host of urologic disease syndromes.

The purpose of this article is to discuss the investigative endeavors which have occupied much of my time during the past twenty years. I would like to start with a few rhetorical questions.

1. Why does a patient with a carbuncle of the skin and sepsis continue to be ill despite antibacterial medication until the abscess is incised and drained? Why does incision and drainage effect cure without the use of any antibiotics or chemotherapy? What has the drainage of the carbuncle reversed in the physiopathologic process (pus and bacteria are still present after drainage but the wound and the patient improve)? The same set of questions can be applied to subdiaphragmatic, perinephric, appendiceal, and pelvic abscesses.

2. The next series of queries relates to operative procedures performed on structures or areas heavily contaminated with bacteria. Why can iatrogenic wounds created in the oropharynx during extensive maxillofacial procedures heal beautifully despite the fact that it is practically impossible to sterilize the oral cavity? The same situation holds true for the large intestine, the gallbladder, and the urinary bladder.

Why can drainage tubes be placed into the bile duct, the kidney, the urinary bladder and, despite the inevitable appearance of pathogenic bacteria in the area, the patient remains afebrile, the tissue is not invaded by the organisms, and the tubes can be kept in place for long periods of time?

On the other hand if the drainage tube is occluded for a period of time, why does fever develop, and sepsis in short order?

3. The last riddle involves the pathogenesis of gram-negative endocarditis and pneumonitis in patients not previously septic and not having operative procedures on the lung or heart?

Herein are cited a series of experimental observations on the urinary tract which might help in answering the questions just posed. Urinary infection has long been the subject of investigation, publication, and discussion, but to this day, as expressed by Cabot and Crabtree in 1916, "there is no subject in which there is so little uniformity of opinion and so much confusion."

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Prevailing Concepts

Some of the concepts prevailing at the present time include (1) urinary infections, particularly in the female, occur spontaneously similar to a cold, and each episode can be treated with antibacterials and without detailed, urologic studies because (2) the bacteria come from the vagina and rectum and ascend through the short female urethra; (3) massage of the urethra during intercourse helps to introduce bacteria into the urethra and bladder; (4) residual urine and stasis due to incomplete bladder emptying provides a wonderful culture medium for bacterial growth; (5) many kidney infections are primary and descend to the bladder; (6) most urinary infections in girls are due to congenital abnormality of the ureterovesical valve leading to ureteral reflux; (7) instrumentation of the lower urinary tract is a common cause for urinary infection because bacteria are carried into the bladder from the urethra; (8) obstructions, large or minor, obvious or obscure, are the major causes of urinary infections, and so forth.

Despite the general belief that most bacteria have their origin in the urethra, no one has been able to demonstrate that the Escherichia coli group of organisms are normal inhabitants of the urethra nor demonstrated the mechanism whereby, in some patients, the bacteria enter the urethra and bladder and remain there to multiply and cause cystitis.

Experimental Observations

Approximately fifteen years ago we became aware of several phenomena which were at variance with these concepts. Our observations began with a middle-aged man with recurrent bladder papillomas who underwent endoscopy every three months. His urine was negative for bacteria without medication and despite the repeated instrumentation. After several years of uneventful regular endoscopic examinations, he suddenly appeared with signs and symptoms of acute cystitis, the onset occurring approximately six weeks after an instrumentation. He was treated for this lower urinary tract infection which cleared and was continued on his bladder follow-up regimen. The patient experienced several more episodes of cystitis including one with an associated unilateral pyelonephritis.

He was finally subjected to a complete urologic evaluation and found to have a vesical neck contracture associated with a mild decrease in size and force of urinary stream, moderate trabeculation of the bladder, and *no residual urine*. A transurethral prostatectomy was performed, and, to this day, the patient has not had another urinary tract infection despite the fact that he continues to have repeated endoscopic checkups for bladder neoplasm.

Many more men were seen with recurrent bacteriuria and cystitis who fell into the same category with mild lower urinary obstruction with no residual urine and who were completely relieved of further attacks of infection after prostatectomy. Interestingly, some of these individuals were in the fourth and fifth decades of life and had been treated for acute and chronic prostatitis over prolonged periods by their physicians.

These cases stimulated some thinking on our part for here we had a group of people who voided with overtly fair urinary streams and had no residual urine but in whom recurrent bacterial cystitis still developed and on occasion associated pyelonephritis. All of them were relieved permanently of their recurring episodes by a prostatectomy. What had the prostatectomy altered? Certainly it did not change the volume of residual urine for it was negligible preoperatively, and the force of the urinary stream was also not remarkably increased. The only obvious factor was a postoperative decrease in intravesical pressure during voiding; this phenomenon had been observed by us and many other investigators over the years. The next question that arose was "how and why does increased intravesical pressure lead to bacterial cystitis?"

While conducting our studies on the adult males, we were also busy trying to diagnose and treat recurrent urinary tract infection in girls. Again we were impressed with the number of children who had recurrent cystitis without abnormal residual urine volumes. A few of these children with obvious lower urinary obstructive uropathy due to meatal stricture of the urethra were also cleared of their recurrent urinary tract infection by relief of the obstructing factor. Again the only obvious facet changed was intravesical pressure, and again its role in the mechanism of urinary tract infection was questioned.

At that time we were aware of some women and children with recurrent urinary tract infection who, for one reason or another, were flagrant infrequent voiders. Some of these patients were cured by being placed on a regimen of

frequent voiding. Although these patients did not have increased intravesical pressure during voiding and no residual urine, many did present with abnormally large bladder capacity. Here the question arose as to the mechanism whereby overdistention of the bladder predisposed to cystitis and its prevention protected against urinary tract infection.

Another set of circumstances involved a large group of patients with transverse myelitis who had been subjected to cutaneous vesicostomy. Although all of these patients have bacteriuria and some carry moderate amounts of residual urine, cystitis and pyelonephritis are relatively rare. These findings are in distinct contrast to the incidence of cystitis and pyelonephritis in some of the paraplegics who void with or without residual urine. Again, the primary difference between the two groups of patients is intravesical pressure for, in the vesicostomy, urine drains from the bladder at low pressures, while, in the voiding paraplegic, high pressures may obtain with powerful reflex contractions associated with spasm of the periurethral striated muscle or by forceful straining.

Finally we might mention a large segment of patients with prolonged tube drainage of some part of the urinary tract (pyelostomy, nephrostomy, ureterostomy, cystostomy) who have a constant bacteriuria but remain relatively free of tissue involvement and sepsis unless the catheter becomes obstructed and intraluminal pressure and/or overdistention of the organ occurs.

Role of Ischemia

An understanding of the part played by increased intravesical pressure and overdistention in urinary tract infection can be gained by reviewing Mehrotra's work.[1] He described a series of experiments performed on female rats in which he transilluminated the posterior wall of the urinary bladder and simultaneously examined the circulation in the anterior wall with a microscope. The rat bladders were distended with varying amounts of fluid and under different degrees of pressure. Mehrotra observed that circulation in the bladder wall comes to a standstill during a strong voiding contraction but resumes with relaxation of the muscle. The flow of blood through the vessels was noted to be decreased also during momentary elevation of the intravesical pressure and upon distention of the bladder. Prolonged increased pressures or distention not only caused decreased blood flow but also produced obstruction in the lumina of capillaries, arterioles, and venules by clumps of erythrocytes with resultant small extravasation of red blood cells in the wall. Eventually the hemorrhages became more extensive and numerous with gross bleeding into the bladder cavity. When bacteria or India ink was administered intravenously, it was observed that both settled out in the hemorrhagic areas; no localization was observed in the bladders of control rats.

Similar findings of decreased blood flow through the bladder wall of dogs with overdistention were observed in the experiments conducted by Finkbeiner and Lapides.[2] Thus it would appear that increased intravesical pressure and/or overdistention of the bladder may predispose to infection by causing ischemia and stasic changes in the small vessels of the bladder and making it susceptible to invasion by bacteria.

That distention of an organ does lead to a decrease in blood flow has been demonstrated by many investigators in experiments on the intestine. In addition, the decrease in blood flow has been related to various types of colitis found associated with colonic obstruction, carcinoma of the colon, Hirschsprung disease, ulcerative colitis, and enterocolitis.

Andriole and Lytton[3] demonstrated vividly that intradermal staphylococcal infection in guinea pigs is markedly enhanced by increases in tissue pressure. The elevated tissue pressure was shown to cause a reduction in intradermal capillary blood flow associated with a decrease in the number of polymorphonuclear leukocytes in those lesions subjected to increased pressures. They postulated "that increased pressure exerts its effect in enhancing pyogenic infections by delaying the delivery of leukocytes and possibly other antibacterial agents necessary for adequate host defenses."

What additional evidence do we have at the present time which suggests that decreased blood flow to an organ predisposes to infection by bacteria from the gut? It has been observed by many investigators that to induce E. coli pyelonephritis experimentally, it was necessary to ligate partially the ureter of the affected kidney before invasion by the gram-negative bacillus would occur. Some observers believed that the physiopathology of bacterial invasion was related to stasis of urine produced by the obstructive ligature. Others believed that it was related

to decreased blood flow through the kidney caused by the increased intrapelvic, intracalyceal, and intratubular hydrostatic pressure. This postulation was supported by the work of Juriansz, Haralampides, and Jeffs[4] who were able to produce bacterial pyelonephritis in dogs by clamping the renal artery for ten minutes and injecting bacteria into the artery distal to the clamp; this result was accomplished without any interference with the pelvis or ureter or by causing stasis of the urine.

Bacterial Routes

The final piece necessary to complete the jigsaw puzzle of urinary tract infection involves demonstration that bacteria can move from the colon to the urinary tract. Early investigators, including Crabtree, Story, and many others, showed that in many cases of urinary tract infection the same strain of organisms could be isolated simultaneously from the urine, bowel contents, blood, and in some cases, the kidney.[5] This was such a strongly held concept that many physicians attempted to treat urinary tract infections by trying to find and correct intestinal lesions. There are reports in the literature indicating that the intestinal flora can cause endocarditis, pneumonitis, etc., and it is obvious that the portal of entry is by way of the blood stream. Feller[5a] has noted that in many patients with extensive burns gram-negative bacillemia develop when their general state of health deteriorates.

A number of studies published during the past several years have demonstrated that transient bacteremias are associated with barium enema, nasotracheal suctioning, sigmoidoscopy, upper intestinal endoscopy, liver biopsy, sigmoid biopsy, etc.

To summarize our discussion thus far, we believe that the normal human male or female is constantly being subjected to episodes of transient bacteremias originating in the intestinal tract. Ordinarily the bacilli are present in the blood stream only for a short period of time because of the recticuloendothelial system and the activity of antibacterial factors present in the blood. However, if a tissue in the body loses some of its antibacterial defenses by virtue of disruption of its structural integrity or by a decrease in its blood supply, then the organisms floating around in the blood or lymphatic streams can gain a foothold in that tissue and multiply to produce disease.

Thus, in the urinary tract, stones, neoplasms, parasites, foreign bodies, and instrumentation can traumatize or disrupt tissue integrity so that a urethritis, cystitis, ureteritis, or pyelonephritis can result by direct invasion of that tissue from organisms in the blood stream or from the skin or mucosal surfaces via the lumina of the urinary conduits.

Blood supply to the organs of the urinary tract can be diminished by diseases involving blood vessels such as diabetes mellitus and severe arteriosclerosis. A more common mechanism for reducing blood supply to the tissues of the urinary tract involves increasing intraluminal pressure or overdistending the organ so that its blood vessels are compromised. This physiopathologic mechanism, in our opinion, is responsible for most urinary tract infections in male and female, young and old. In the male, it is primarily the obstructive abnormalities such as stricture, prostatism or valves; and neurogenic bladder disease which compromise blood flow; while in the female, as we shall see, poor or abnormal voiding patterns account for most of the upper and lower urinary tract infections.

Urinary Tract Infections in Females

With the crystallization of our ideas on urinary tract infection and the evolvement of the concept just described, we decided to investigate a group of women and female children with documented recurrent infection in an effort to determine the causes for their infection and the results of appropriate therapy.[5]

A group of 250 women and 71 girls with a documented history of recurrent urinary tract infection was subjected to complete medical and urologic diagnostic studies. Particular attention was paid to voiding habits throughout life, including frequency of urination, urgency, and incontinence.

Diagnostic examinations included excretory urography, voiding cystourethrography, endoscopy, urethral calibration, and cystometry. Presence of infection was determined by urinalysis.

Evaluation of the results of the examinations revealed that the majority (66 per cent) of the adult patients were infrequent voiders, urinating once in five to ten hours and exhibiting bladder capacities greater than 500 ml. in many instances. One of 6 patients demonstrated the

incompletely controlled infantile or uninhibited neurogenic bladder while the remainder evidenced bladder neoplasm, urethral meatal stricture, etc. It was obvious from the data that by far the most important etiologic factors associated with recurrent urinary tract infection in the adult female were infrequent voiding and the uninhibited neurogenic or infantile bladder.

Incidentally, a recent study by Seskie and Diokno[6] on urinary tract infection during pregnancy revealed that most of the women had recurrent episodes of cystitis prior to insemination and a history of flagrant infrequent voiding. Their difficulties during pregnancy were merely a continuation of their prepregnant urinary illnesses.

The reasons given for infrequent voiding were most interesting and revealing, particularly to the male who has never paid much attention to the subject. The explanations included: (1) too busy with occupation or housework to "take time out" for urinating; (2) boss frowns on trips to restroom during working hours; (3) too few toilets for number of people desiring to use them at their place of work or at various shopping areas; (4) fear of contracting venereal disease, Trichomonas infestation, etc., from facilities in public rest rooms; (5) sense of modesty restraining individual from leaving the room in a social gathering; (6) believed that the longer one held her urine, the stronger her bladder would be and the better it would be for her general well-being; (7) believed that learning to hold urine for a long time made for a better traveler; and (8) difficulty in removing neck to thigh foundation garments in public rest rooms to urinate without soiling one's self.

The studies on the girls showed that infrequent voiding and the infantile bladder were the causes for recurrent infection in more than 90 per cent of the group. They differed from the adult females in that the uninhibited neurogenic bladder occurred in the majority of girls with recurrent urinary tract infection (61 per cent) rather than infrequent voiding. Obstructive uropathy was present in less than 3 per cent of the children.

The patients were treated with appropriate antibacterial medication for a period of two to three weeks and simultaneously placed on a regimen of voiding every two hours during the day and to awaken once or twice at night to empty their bladders. They were advised not to force fluids but rather to restrict intake. Cholinergic therapy was used to stimulate decompensated bladders with abnormal residual urines in the case of the infrequent voiders, while anticholinergic treatment was employed in the individuals with severe uninhibited neurogenic bladders.

The majority of the children and adults responded to therapy with clearing of their urinary tract infections and absence of recurrent episodes. Those in whom further infections developed were usually found not to have adhered to the regimen of frequent urination. No operative procedure was performed for ureteral reflux in any of the patients. At that phase in our studies, we considered ureteral regurgitation to be a phenomenon usually secondary to the various causes for urinary tract infection and of no import provided the primary cause was treated. In our patients many of the cases of ureteral reflux vanished with eradication of the infection.

However, as our experience increased, we learned that some of the patients with moderate to severe ureteral reflux persisted in having recurrent episodes of acute pyelonephritis despite physiologic voiding regimens. Close observation of these individuals revealed that they engaged in strenuous physical exertion with generation of high intravesical pressures. To cure these physically active people of their debilitating episodes of pyelonephritis, we found it necessary to reimplant their ureters using antireflux techniques.

Physiopathology of Infection with Uninhibited Bladder

At this point I believe that it would be appropriate to elucidate the mechanism involved in the occurrence of bacterial cystitis in patients with the incompletely controlled infantile or uninhibited neurogenic bladder since this is by far the most common cause for most urinary tract infections in girls and which should be treated by medical means rather than surgical procedures.[7]

Uninhibited or uncontrolled voiding contractions of the urinary bladder are present in all infants, and periodic incontinence is a normal occurrence. As the bladder fills with urine from the ureters, proprioceptive endings in the bladder wall are stimulated by stretching of bladder muscle to send sensory impulses along the afferent limb of the reflex arc. The sensory impulses impinge eventually on the lower motor neurons to the detrusor and stimulate them to send motor impulses along the efferent limb of the

reflex arc to cause a coordinated contraction of the bladder and urethral smooth muscle; concomitantly there is a reflex relaxation of the periurethral striated muscle. The end result is immediate evacuation of the urinary bladder with a forceful stream and at relatively low intravesical pressures.

Urinary tract infection is absent in the normal infant. As the child's nervous system maturates, cortical control over both bladder smooth muscle and periurethral striated muscle is gained by the age of two to three years, and the child is said to be "toilet-trained." Urination is initiated and inhibited voluntarily by direct cortical control over bladder smooth muscle via the corticoregulatory tract. The cystometric examination will disclose no uncontrolled contractions of the bladder and intravesical pressure will be low when the bladder is full and the individual has a desire to void. At the start of and during urination the periurethral striated muscle is relaxed, either voluntarily or reflexly, and micturition occurs at relatively low intravesical pressures. No urinary tract infection is present in the normal child.

In some girls cortical control over bladder smooth muscle is not attained at the age of three as evidenced by uninhibited contractions on cystometric examination. However voluntary control of the periurethral striated muscle is developed. Thus when the bladder of one of these children fills with urine, uncontrolled contractions of the detrusor occur associated with a desire to void. If the child voids immediately, intravesical pressures remain low and no urinary tract infection occurs. But should the child attempt to prevent urination and hold her urine for awhile, a marked rise in intravesical pressure will occur. The increase in intravesical pressure develops because the bladder muscle is contracting forcefully and involuntarily in an attempt to evacuate the bladder while simultaneously the child is trying to prevent incontinence by voluntarily contracting the periurethral striated muscle to cause elongation and constriction of the posterior urethra or urinary sphincter.

It is exactly the same mechanism as the dyssynergia between the detrusor and external sphincter found in some of the spinal cord injury patients; the only difference being that the external sphincter or periurethral striated muscle in paraplegics is contracting reflexly in an uncoordinated fashion while, in girls, the external sphincter is voluntarily contracted to close the urethra. The end result is the same — a urethra closed to the expulsion of urine by the contracting bladder with resultant abnormally high intravesical pressures.

Obstructive uropathy caused by prostatic disease or urethral stricture owes its bad effects to the same general process, namely, a bladder contracting against a closed or narrowed urethra. In this instance the detrusor contraction is voluntarily initiated; the external sphincter is relaxed in a coordinated fashion, but the conduit is closed or narrowed by a structural abnormality (hyperplastic prostate, vesical neck contracture, etc.). All three situations result in high intravesical pressures which may lead to ischemia, cystitis, pyelonephritis, hydroureteronephrosis, ureteral reflux, trabeculation of the bladder, and diverticula.

Intravesical pressure studies of patients with normal bladders and with uninhibited neurogenic bladders support fully the physiopathology proposed for the high pressures developed in the uncontrolled bladder. As postulated previously, the high intravesical pressure decreases blood flow to the bladder tissue and makes it susceptible to bacterial invasion.

The successful results in eradicating urinary tract infection in both male and female in accord with the concepts proposed in this discussion, prepared and emboldened us to treat certain urinary abnormalities in a most heterodoxic fashion. To reiterate we postulate that most cases of urinary tract infection are due to some underlying structural or functional abnormality of the urogenital tract which leads to decreased resistance of tissue to bacterial invasion. The most common cause for increased susceptibility to bacterial invasion is decreased blood flow to the tissue brought about by increased intraluminal pressures or overdistention of the organ. The resulting ischemic tissue is thus prey to invading organisms from the patient's own gut via the hematogenous or lymphogenous route. Transient bacteremia is believed to be a common phenomenon in healthy individuals.

Clinical Application

Self-catheterization

Thus the key to prevention of urinary tract infection is the maintenance of a good blood supply to the urinary tract. It follows that residual urine per se and organisms ascending through the urethra are of doubtful importance in the genesis of urinary tract infections. As a

corollary, bacteria introduced into the bladder through the urethra by a catheter or instrument should be destroyed by the normal bladder tissue provided the instrumentation is transient. Viewing the proposition in another light, persistent urinary tract infection occasioned by abnormal bladder function either on a neurogenic or obstructive basis, should be amenable to eradication on condition overdistention of the bladder and abnormal intravesical pressures are obviated. Theoretically, intermittent, urethral catheterization preventing these abnormal conditions and establishing a healthy, resistant bladder tissue, should lead to cure of the infection. The startling aspect of the concept from the aseptic point of view, holds that the catheterization need not be performed in a sterile fashion.

It was on this basis that we instituted a study eight years ago to investigate the efficacy of clean, intermittent self-catheterization in the therapy of infection associated with atonic bladder, neurogenic bladder, and obstructive uropathy not amenable to operative correction.

In 1971 we published our first report involving 14 patients on a self-catheterization program and observed that the regimen resulted in tremendous improvement in the urinary tract abnormalities of these people including urinary retention, incontinence, infection, and mental difficulties. The procedure obviated the need for surgical procedures designed to correct outlet obstructions and to divert the urine. We concluded the article with the statement, "The fact that clean, intermittent self-catheterization helped eradicate urinary infection and maintain a sterile urine for prolonged periods lends further support for our concept of the physiopathology of most urinary infections."

A three-year follow-up on 100 patients using clean, self-catheterization was reported in 1973, and a five-year follow-up on 218 people in 1975.[8] We are now preparing an article on the seven-year follow-up of 304 individuals and are pleased to state that clean, intermittent self-catheterization continues to be a safe, highly effective form of treatment for a wide variety of urinary tract disorders. More than 600 patients have been entered into the University of Michigan Medical Center self-catheterization program since its initiation in 1970.

Self-dilatation

Our experience with clean, intermittent self-catheterization led us to utilize the technique in the treatment of urethral stricture. When we learned that the normal human male is able to catheterize himself many times a day, without experiencing pain, producing sepsis, or injuring himself, we decided that clean, intermittent self-dilatation with a 24 F Robinson catheter following internal urethrotomy might be a good form of conservative therapy; and, indeed, it has far exceeded our expectations.

By starting the patient on self-dilatation a day or two after urethrotomy, the physician obviates the complications and disadvantages of the stent lying in the urethra for six to eight weeks; or the cost, discomfort, and septic episodes of weekly or semiweekly urethral dilatations in the office.

A number of our patients have been followed for years and have been noted to be free of infection on no medication; to need fewer visits as outpatients; and to require no additional hospitalizations for further internal urethrotomies. In some cases clean, intermittent self-dilatation of the urethra with a catheter was discontinued after a few months because the diameter of the urethral lumen became fixed at a large caliber.[9]

Transurethral diverticulectomy

Another opportunity to employ the concept that increased intraluminal pressure or overdistention predisposes to infection and sepsis, and that abolition of high pressure and overstretching reverses the processes, presented in a female with persistent or recurrent urethral diverticulitis following a transvaginal diverticulectomy. We postulated that a freely draining urethral diverticulum per se was innocuous and that it reached the clinical horizon only when it became occluded and distended. The resulting increased intracavitary pressure would impair blood flow through the wall of the diverticulum and predispose to bacterial invasion and inflammation of the diverticulum. Pain would develop on the bases of infection and distention of the diverticulum. As a corollary permanent decompression of the diverticulum should relieve the pain almost immediately, improve blood flow, and aid in the eradication of the infection; the urethral diverticulum or diverticula need not be excised.

Over the past seven years we have operated on 6 women with persistent urethral diverticulitis following one or more attempts at transvaginal diverticulectomy in 5 and transurethral in 1. We have employed an operative technique for "laying open" the cavities of urethral diverticula via the urethra utilizing a resectoscope

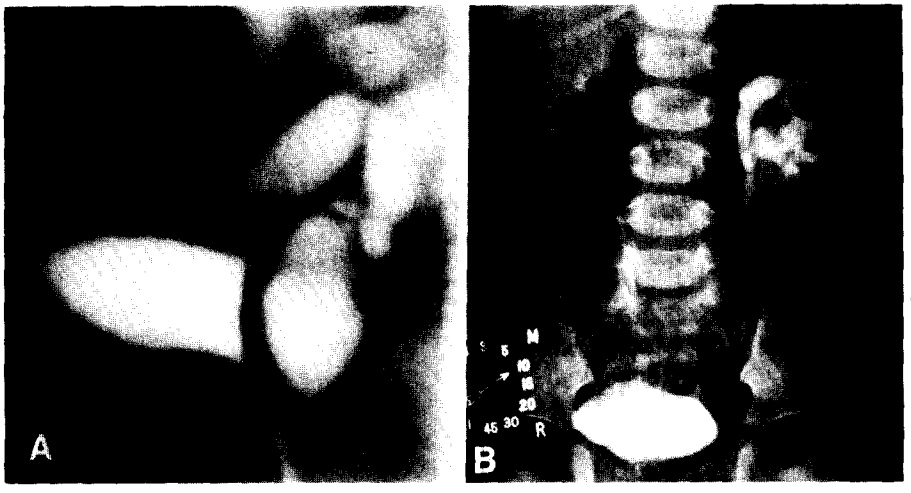

FIGURE 1. *(A) Retrograde urethrocystogram demonstrates urethra, bladder, and tortuous dilated ectopic left ureter emptying into proximal urethra. (B) Excretory urogram shows excellent opacification of duplicated left kidney following left ipsilateral ureteroureterostomy and partial ureterectomy of left ectopic ureter.*

with a knife electrode.[10] The procedure involves urethroscopy and the insertion of the knife electrode through the diverticular stoma, and progressive incision of the "roof" of the diverticulum or "floor" of the urethra in a linear fashion until the entire roof is divided and the cavity laid open. When there are multiple diverticula, the orifice of each diverticulum is widened in a similar fashion.

All of the patients have been relieved of their symptoms and infection. There have been no cases of urinary incontinence or long-term recurrence. The length of stay in the hospital varied from one to four days, with an average of 2.3 days.

Ectopic ureter

The most recent application of the basic principles relating to urinary tract infection involved a baby girl who was first hospitalized at the age of two and one-half months and eventually diagnosed as having pulmonary artery stenosis, atrial septal defect, duplication anomalies of both kidneys with an ectopic left ureter opening into the most proximal segment of the urethra (Fig. 1A). When the infant was initially seen, she had a urinary tract infection and was not symptomatic from her cardiac lesion. Because of the persistence of her infection, a partial ureterectomy of the proximal portion of the dilated ectopic ureter was performed and the upper pole pelvis connected to the ureter of the lower pole collecting system via an ipsilateral ureteroureterostomy (Fig. 1B). The distal ectopic ureter was left in place with the anticipation that the remaining segment of ureter would be removed later at a more propitious time.

However cyanosis began to develop, and it was deemed necessary by the cardiac consultants that a corrective operation on her heart be performed almost immediately. Her urine was being kept sterile with antibacterial medication, and a decision was made to operate despite the presence of the dilated distal ectopic ureter which was functioning as a diverticulum of the urethra. The infant tolerated cardiac surgery well and was continued on antibacterial medication for sixteen months postoperatively. Because her urine had remained sterile throughout her long postoperative period and her heart was well healed, it was decided to wean her of her medication and observe her course. Theoretically we believed that her urine should remain sterile if the dilated segment of ectopic ureter drained freely into the urethral lumen and did not become overdistended. The child is now one and one-half years following discontinuation of her medication, and her urine has remained sterile throughout. She voids in a normal fashion, is continent, and the ectopic distal ureter remains.

Synopsis

In summary I would like to list the principle points we have attempted to make:

1. Infection anywhere in the body is the result of interaction between organism and host.
2. Insofar as the urinary tract is concerned, it is host resistance which is the determinant of infection rather than the organism which is quite ubiquitous.
3. The bacteria most commonly invading the urinary system have their origin in the patient's own large intestine and may be found in the vagina, oropharynx, urethra, blood stream, lymphatics, and on the skin.

4. Most urinary tract infections begin as a cystitis secondary to decreased host resistance brought on by disruption of tissue integrity or a decrease in blood supply to the bladder.
    A. Trauma, neoplasm, foreign, bodies, parasites, and granulomatous processes affect tissue intactness.
    B. Vesical overdistention and high intravesical pressures decrease bladder blood flow and resistance to infection.
5. In the normal and pregnant female infrequent voiding and the uninhibited bladder are the most common causes for urinary tract infection and are best treated by institution of healthy voiding regimens.
6. Urinary tract infection in the male is frequently associated with high intravesical pressures secondary to both structural and functional obstructive uropathy and is alleviated by lowering the intravesical pressure through either surgical or medical measures.
7. The concept of the primary importance of host resistance in infection, has permitted the introduction and use of clean, intermittent self-catheterization; clean, intermittent self-dilatation; and transurethral diverticulectomy in the treatment of a host of urologic disease syndromes.

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