INTERSTITIAL CYSTITIS

WILLIAM J. ENGEL, M. D.

Although there are numerous reports in the literature dealing with the subject of interstitial cystitis, our experience justifies the statement that this disease is recognized too infrequently by the general profession, and that patients are too commonly subjected to diverse surgical attacks in a futile attempt to remove a most distressing pain, or even worse, they are classified as neurotics and denied proper investigation.

This disease was first described by Hunner in 1914, and therefore is frequently referred to as Hunner's ulcer, but it has also been termed submucous cystitis, panmural cystitis, elusive ulcer, etc. *Interstitial cystitis,* however, is a more descriptive title. Although originally described as a rare type of bladder ulcer, increased recognition has shown that it is not an infrequent lesion, and in the past fifteen years we have encountered 70 cases. It is preponderately a disease of females, 90 per cent of our cases having occurred in this sex. The majority appeared between the ages of 40 and 70, the extremes in our cases being 18 and 77 years of age. Of the 63 women, 10 were unmarried, while of the 53 who were married, 31 had borne children and 22 had not.

The etiology of this disease is quite unknown. In his original paper, Hunner suggested that focal infection might be the cause, and Bumpus and Meisser reported that they had reproduced the lesion in the bladders of rabbits injected with cultures obtained from the teeth and tonsils of patients suffering from the disease. Later, Moensch and Counsellor reported similar results using cultures obtained from the infected cervix of a patient suffering from the disease. They felt that, because of the preponderance of the lesion in females, infection in the cervix was a logical focus to explain the disease. However, the theory of focal infection has not been borne out in clinical experience and we have seen no patients cured by the removal of questionable foci. Others have felt that the disease was the result of previous attacks of cystitis, but in our group of cases no consistent history of antecedent inflammation of the bladder could be obtained. In only 12 cases was there any evidence of urinary infection at the time of examination at the Clinic.

Certain clinical and pathological features suggest that the bladder lesion is due to impaired circulation which might be caused by a vascular disease or nutritional deficiency. Whatever the cause, it would appear that it is part of a general process, the bladder lesion being only a local manifestation of the disease. In this connection, it is interesting to note that in one of our most severe cases there was also fibrosis and contraction of the sartorius muscle. Our ophthalmologist in examining the conjunctival capillaries in a few cases is of the impression that there is a diminution of the capillary bed.

In most instances one can almost make a diagnosis from a careful history. The long duration of symptoms is notable; in only three of our 70 cases had the symptoms been present less than a year and in one instance they had been present for 16 years. The chief complaint is frequent urination and the associated symptom is pain. In many instances the frequency is clock-like, it being necessary to empty the bladder at perfectly regular intervals, day and night. In certain cases the patients have related that they can almost tell the time at night by the regularity of the periods at which they have to arise. In this connection it is well to mention that nocturia is a *requisite* in the diagnosis, for without it the lesion does not exist, and this fact serves well in differentiating interstitial cystitis from other conditions producing diurnal frequency. The pain is usually suprapubic in the bladder area but may be in either lower quadrants of the abdomen, the groin, the vagina, perineum, or the rectum. It may be described as a knife-like pain or a burning distress, which reaches its maximum intensity when the bladder is distended with urine. Voiding usually brings temporary relief but the discomfort returns as soon as the bladder fills again. The pain is aggravated by motion, particularly jarring such as may be produced by riding in a motor car. Long years of suffering induces in these patients a severe nervous condition.

If the history contains the above features, one should always suspect interstitial cystitis. The frequent errors in diagnosis usually result from the fact that urinalysis in these cases is entirely negative and this tends to obscure the diagnosis. Equally confusing to the examining physician is the fact that very commonly, bimanual pelvic examination will reveal the presence of exquisite pain and tenderness to palpation, which may lead to a diagnosis of some type of pelvic disease for which operation is advised. It is interesting to observe that in 17 of our 70 patients previous operations on organs other than the bladder had been carried out without relief of the symptoms.

Although the diagnosis must finally be made by cystoscopic examination, it can be virtually established by introducing a catheter into the bladder and filling it to capacity. If this capacity is found to be small (less than 150 cc.) and if slight overdistention tends to reproduce the patient's pain, the diagnosis is presumptive, while if more vigorous overdistention is followed by a small amount of blood one may almost be certain of the diagnosis. These findings, of course, hold only for the typical case.

The cystoscopic picture is somewhat varied, but in general three types may be recognized: First, there may be early, diffuse involvement of the bladder without ulceration. In these cases one first observes that the capacity of the bladder is definitely limited. Careful examination fails to reveal any typical ulcer but one is impressed with the smooth

bladder mucosa which is unusually pale, and with the abnormal distribution of the vessels. The vessels in such cases are much shortened, having a fragmented appearance, and they seem to appear suddenly and then disappear with equal abruptness. Means terms this a pre-ulcer state but, although I have recognized this type in seven instances, I have never seen one go on to the development of a typical ulcer.

The second type is that which presents the more or less typical single or multiple, discrete, linear ulcer. This is the most common type and 52 or 74.3 per cent of our cases fell into this group. The ulcer is frequently very small and may escape detection unless the cystoscopist is looking for it. It is always on the movable portion of the bladder and quite frequently on the dome in the vicinity of the air bubble. I have never seen an ulcer on the fixed portion of the bladder, and believe that it never occurs. The typical lesion is first brought to the attention by its rather characteristic salmon-pink color. On closer inspection, this area is found to have a rather puckered or contracted appearance, creating a minute ridge on the summit of which is a linear, superficial, so-called ulcer, which is frequently covered with a faint white exudate. Although occasionally single, most of our cases have presented two or more such lesions. When such areas are touched with a ureteral catheter, they are found to be exquisitely painful and the patient immediately recognizes it as the pain she has been suffering. Forceful distention of the bladder provokes a most characteristic superficial splitting of the mucous membrane, followed by a trickle of blood which arises from multiple pinpoint sources. Frequently these lesions will be found in a bladder which otherwise appears perfectly normal, while in many cases the unusual distribution of blood vessels previously described will be seen in the adjoining mucosa.

The third type is the late ulcerative and contracted stage which was present in eleven, or 15.7 per cent of our cases. In this type, the bladder capacity is so markedly reduced that frequently it is impossible to carry out cystoscopy without anesthesia. Even then, the introduction of perhaps 30 to 50 cc. of solution will precipitate so much bleeding that accurate visualization of the bladder may be impossible. In such cases the entire bladder is involved with multiple areas of ulceration and fibrosis. To me, this type presents the greatest difficulty in diagnosis and it must sometimes be made by exclusion.

In the differential diagnosis, one must consider tuberculous cystitis, early infiltrating carcinoma, and radium ulcer. Since infection of the upper urinary tract must be ruled out in all cases, it naturally follows that differentiation from tuberculosis offers no particular difficulty. Although rarely confused with carcinoma of the bladder, biopsy examination should be employed if any doubt exists. The lesion produced by application of radium to carcinoma of the cervix may closely resemble

interstitial cystitis, but a history of radium treatment solves this problem. Thus there is ordinarily no difficulty in making the diagnosis in the first two types, providing the examiner has considered it as a possibility. Although the third type presents more difficulty, careful study will rule out all other possibilities.

The pathological picture seen in this disease conforms rather accurately with the cystoscopic findings which have been outlined. The mucous membrane is thin or absent, the normal transitional epithelium having changed to a single layer of flattened or cuboidal cells and there may be a very slight depression at the site of the actual ulcer. There is loss of the capillary bed which causes the larger arterioles to stand out prominently, and these have increased thickening of their walls. There is markedly increased thickening and fibrosis of the submucosa, with actual sclerosis in certain areas, which may even extend into the muscular layer. In many cases there will be, in addition, some lymphocytic and plasma cell infiltration, especially around the blood vessels.

Many methods of treatment have been advocated for the relief of this disease. Among the nonsurgical procedures, I mention irrigation of the bladder with silver nitrate solution, hydrostatic distention of the bladder, local application of pure phenol, and fulguration of the ulcer. More recently, Folsom has reported some favorable results from the injection of absolute alcohol into the ulcer bearing area. Any one of these procedures may be expected to afford a certain amount of relief.

The vast majority of our patients have been treated by a combination of hydrostatic distention plus fulguration under anesthesia. I feel that deep coagulation and extensive destruction of tissue is inadvisable and it has therefore been my practice to produce only the most superficial coagulation, using a large surface ball type of electrode. This is merely brushed over the ulcer in such a way as to produce only the most superficial blanching of the tissues. When this has been done, one notes a definite increased redness of the surrounding tissues with dilatation of the vessels. I believe the beneficial results are due to this increased vascularity stimulated by the lightest fulguration. The immediate result of this treatment is often miraculous, for even on recovering from the anesthesia the patient may express herself as feeling relieved and passes the first night in many months without arising to void. Recurrence of symptoms, however, is unfortunately the rule, the intervals of comfort ranging from three months to a year. In only three cases have I effected a cure as judged by relief of symptoms and disappearance of the ulcer, but all patients have been improved and the relief is so gratifying that they are satisfied to report every three to six months for repetition of the treatment.

Among the surgical procedures advocated are partial resection of the bladder, pre-sacral nerve resection, and ureteral transplantation. Hunner

originally advised resection of the ulcer bearing area of the bladder but later reported a high recurrence. This coincides with our experience, for we resected the ulcer in five cases with recurrence of symptoms in all instances. I believe this operation has been rather generally discarded.

Pre-sacral nerve resection, based on good theoretical principles, has yielded very disappointing results. Learmonth and Braasch reported the results of this operation for certain diseases of the bladder, eight operations having been done for interstitial cystitis. They considered only one patient cured and this one had, in addition, a resection of the ulcer. Quinby reported no relief in three patients in whom he resected the pre-sacral nerve. We have not performed this operation, but in two patients we have injected the paravertebral sympathetic chain. Although both patients obtained physiological effects as measured by increased temperature in the extremities, neither had the slightest relief of bladder symptoms. These facts constitute the chief argument against the conception that this is a primary vascular disease, especially one of the vasospastic type.

Ureteral transplantation should be considered a last resort, and should not be advised until one has exhausted more conservative efforts. It is indicated only in type three, where there is extensive ulceration and contraction of the bladder. We have carried out this operation on five patients, and the two who survived the operation have been entirely comfortable and happy, both regretting that they did not have it done sooner. No better statement of the indication for the operation could be given than a brief history of one of these patients.

A woman, 42 years of age, presented herself at the Clinic in April, 1931, complaining of having to void every 15 to 20 minutes; this was associated with suprapubic pain. She had had a hysterectomy without relief, and extensive bladder treatments with only slight temporary improvement. Examination showed a very nervous, undernourished woman, whose bladder capacity was 60 cc. Cystoscopic examination revealed a generalized ulceration and contraction of the bladder, which bled freely with overdistention. The upper urinary tract was normal. Treatment over a period of several months with distention and fulguration produced only meager results, the greatest capacity of the bladder being four ounces. It is difficult to describe this patient's misery, but suffice it to say that at times life was almost intolerable. We suggested to her the possibility of ureteral transplantation but she had planned a trip to Scotland and wished to postpone operation, so in a period of relative comfort she started her trip. On arrival in New York, however, her symptoms became very intense, and she consulted a surgeon who admitted her to the hospital and did a unilateral nephrostomy, advising that the other side be done later. This was not done, however, and insisting on her trip, the patient sailed from New York with a nephrostomy drain-

age. On arrival in Scotland, she consulted a physician who treated her for a time, and then she consulted a urologist in Edinburgh who advised and carried out a resection of the pre-sacral nerve. In the meantime, the kidney incision had healed, but she derived no benefit from the nerve resection and eventually returned to this country with bladder symptoms as bad as ever. By this time she was willing and anxious to have ureteral transplantation, which was carried out in November, 1933. This was done as a two stage operation, the patient having an entirely uneventful convalescence. She is still well at this date.

This is, of course, an extreme example, and yet it serves well to illustrate the type of case in which we have recommended ureteral transplantation. There are others among the ten cases in type three who should have it done but who have as yet been unwilling to accept the operation.

We have not deemed it necessary to do cystectomy, and this has not been done in any of our patients with ureteral transplantation. With the urinary stream diverted, the bladder becomes a nonfunctioning organ and no symptoms of the disease persist even though the bladder is still present.