THE ETIOLOGY AND PATHOLOGY OF PYELITIS CYSTICA, URETERITIS CYSTICA AND CYSTITIS CYSTICA *

HARRY D. MORSE, M.D., C.M.
Fellow in Urology, The Mayo Foundation

(From the Mayo Foundation, Rochester, Minn.)

Cysts of the mucous membrane of the renal pelvis, ureters and urinary bladder have long been recognized. They rarely produce clinically recognizable phenomena but among pathologists and surgeons their etiology, occurrence and evolution have been much in dispute. This study was undertaken to review and correlate these different opinions.

REVIEW OF THE LITERATURE

In the pathologic work of Morgagni ²⁸ in 1761 is found the first reference to this condition. He reported two cases, one in a man aged 60 and the other in "a decrepit old man who for many years had been afflicted with lues venerea." In both cases there was bilateral hydronephrosis and hydro-ureter. He described his observations in the first case: "on feeling the ureters, the sensation of there being calculi in some parts of them was communicated, but when they were slit open, an hydatid was found in every one of the places. Some were round, others were oval, hanging from the inner coat into the canal of the ureter, but not by a small stalk. The round ones were equal in size to very small grapes and the oval hydatids were double the length of the others."

The next case to be found in the literature was reported by Johnson ²⁰ in 1816. His case was that of a woman; hydronephrosis and hydro-ureter were present on the same side as the cysts.

Rayer, ³⁴ in 1837, and Rokitansky, ³⁵ in 1861, reported cases of this condition. Rokitansky says: "Cysts appear to be more frequent in the urinary passages than they are in and upon other excretory ducts. Without referring to the other cases, we may notice two that have

* Thesis submitted to the Faculty of the Graduate School of the University of Minnesota in partial fulfillment of the requirements for the degree of Master of Science in Urology, June, 1925.

Received for publication September 22, 1927.

been observed in the Vienna Hospital. They represent cysts, the size of millet seeds or peas, developed under the mucous membrane and either grouped together or solitary, containing a colorless or yellowish serous fluid in which is found a soft glutinous or hard nodule varying in size and resembling amber. These cysts and their mucous covering occasionally burst, which is proved by the concretions having been discovered unattached in the bladder. They were chiefly found occupying the ureters and in one case the pelvis and calices of the kidney." Neither Rayer nor Rokitsky expresses definite views as to the origin of the cysts.

Virchow,⁴³ in 1863, described a case and compared the cysts to the mucous cysts of the vagina.

Egli,¹¹ in 1873, in a study of the histology of the renal pelvis, described flat globular glands resembling sebaceous glands, but these were inconstant in their occurrence.

In 1876 Litten²⁴ offered the first microscopic description of these cysts, but failed to see or make note of any cell nests. He was definite in his conclusions that these cysts were formed by an inflammatory blocking of the mucous glands and crypts of the mucous membrane, the retention of the secretion in these glands and crypts forming the cysts.

Hamburger,¹⁵ in 1880, also described glands of the renal pelvis and ureters but stated that they were not a constant structure.

Ebstein,¹⁰ in 1882, reported a case of cysts of the renal pelvis and ureter and supported Litten's views concerning their origin.

Limbeck,²³ in 1887, reported a case of cysts of the ureter. He was unable to find glands in the mucous membrane of the ureter and concluded that the cystic formations in his case were due to the agglutination of the proliferated mucous membrane and also to the central degeneration and liquefaction of sprouts of epithelium from the deeper layers of the mucous membrane. He did not deny that cysts are formed by the inflammatory blocking of mucous glands.

In 1889 Eve¹² published the first article in English literature on this condition. He reported a case and described ovoid bodies constantly found in the colloid contents of the cysts, which corresponded in size and appearance to pseudonavicellae. This observation convinced him of the parasitic origin of these cysts. He was supported in this view by Bland-Sutton,⁵ Clark,⁷ Voelcker,⁴² Pisenti,³² von Kahlden²¹ and Morris.²⁹ In Osler's³¹ textbook, as late as the ninth

edition in 1920, psorospermiasis of the kidneys and ureter is mentioned.

Silcock³⁸ was the only English writer up to 1889 who disagreed with the theory of parasitic origin. He described foci of epidermal cells in which a lumen was formed by degeneration of the central cells.

In the meantime, von Brunn⁶ published his noteworthy article. He described epithelial bodies lying below the mucous membrane. Those showing an epithelial connection with the surface epithelium he designated epithelial buds or sprouts and those showing no connection he designated epithelial cell nests. He stated that these epithelial nests and buds were formed by the downward proliferation of the epithelium in the form of sprouts, and their subsequent separation from the mucosal lining. He believed that this proliferation of the epithelium was stimulated by inflammation. In proof of these statements, he said he was unable to find glandular elements, that the epithelium forming the nests was similar in every respect to the surface epithelium, and there was no constant lumen or exit duct, nor were the changes ordinarily seen in secretory epithelium present in the cells. The cystic formation he believed to be due to the degeneration of the central cells of the nests.

Lubarsch²⁶ shortly afterward confirmed the observations of von Brunn and reported two cases of ureteritis cystica and ten cases of cystitis cystica. He said that the microscopic appearance and the staining reaction of the contents proved that cysts were formed by degeneration of the central cells. In his cases, he found cysts originating in three separate ways: (1) from von Brunn's cell nests; (2) from the inflammatory closure of the crypts of the mucous membrane, and (3) apparently from abnormally placed glands of the upper urethra.

Aschoff³ reported a case of ureteritis cystica and agreed with Lubarsch in his views regarding the formation of cysts from von Brunn's cell nests. He examined the ureters and bladder in a boy aged $1\frac{1}{2}$ years, and a girl aged 3 years, but was unable to find either epithelial buds or cell nests or cysts. On further study, he was unable to find glandular formations above the internal sphincter of the urethra. He concluded that von Brunn's cell nests were of inflammatory origin and showed a predilection for the calices of the renal pelvis, the ureteropelvic juncture and the neck of the bladder. He

believed that these nests of von Brunn were formed in two ways: by proliferation downward of the deeper layers of the epithelium of the urinary tract, and by proliferation of the fibrous connective tissue which grew upward and cut off islands or nests of the epithelium.

Marckwald²⁷ found ureteritis and cystitis cystica in a new-born child and maintained that an inflammatory process was not necessary to the formation of von Brunn's epithelial buds or cell nests.

Stoerk,³⁹ after a thorough study of thirteen cases of ureteritis and cystitis cystica, differed with Marckwald in that he considered the origin of von Brunn's cell nests to be inflammatory. He also disagreed with von Brunn, Lubarsch and Aschoff and considered the cystic formation to be a secretory phenomenon.

Following this, Radtke,³³ Motz and Cariani,³⁰ Liebreich,²² and Harris¹⁶ reported cases and supported von Brunn, Aschoff and Lubarsch in their conclusions.

Herxheimer¹⁷ reported two cases of ureteritis and one case of cystitis cystica. He examined twenty-nine cases without gross cysts, making serial sections from selected situations in three. Von Brunn's cell nests or buds were found in eleven of the twenty-nine cases. Glandular elements were not found. Nests were not present when the subject was less than 2 years of age. In one case, a child aged 8 years, von Brunn's cell nests were found. No parasites were found in the cystic contents and the reaction for mucus was negative. He concluded that von Brunn's cell nests are the origin of the cysts, that they are not normal but are commonly present at any age, that they vary in number, size and distribution, and that they are the result of the proliferation of the mucous membrane of the urinary tract following an inflammatory process. The elimination of toxic substances is enough to cause this proliferation and explains the cell nests and cysts found by Marckwald in the new-born.

Giani¹³ introduced into the bladder of rabbits by a suprapubic incision gelatin capsules containing bacilli of tuberculosis, for the study of tuberculosis of the urinary tract. In some instances the capsule passed from the urethra while in others it formed the nucleus for salty incrustation. On killing these rabbits he discovered a condition similar to cystitis cystica. Following this, he denuded areas of the bladder in twenty rabbits, using a Volkmann curet through a suprapubic wound. He killed the rabbits at different times from

forty-eight hours to two hundred seventy days afterward. Sections taken in forty-eight hours showed only scattered bits of epithelium remaining in the places curetted; in five days, granulation tissue and beginning proliferation of the remaining epithelium were evident; in ten days, the epithelium was spread out, practically covering the whole area; in fifteen days numerous mitotic figures were seen in the epithelial cells; in twenty-five days, epithelial buds or sprouts were present; in forty-five days, epithelial cell nests as well as the epithelial buds were present; in seventy-five days, the center of the epithelial cell nests stained poorly and in places a lumen was seen; in one hundred days, the cysts were increased in size and some were approaching the surface, and, with a magnifying glass, the cysts were just visible on the surface; in one hundred twenty days, the cysts were diminished in number; in one hundred sixty days, the mucosa was practically normal; in two hundred seventy days, all signs of the condition had disappeared. He concluded that any irritation of the mucous membrane will cause proliferation of the epithelium and the formation of von Brunn's epithelial buds and cell nests, and that after the nests have formed they progress to the point of forming cysts and eventually rupture into the lumen of the urinary tract even in the absence of the original irritation.

Since Giani's experiments, many papers have been written on pyelitis cystica, ureteritis cystica and cystitis cystica, and several cases reported. Notable among these were the papers of Stow,⁴¹ Saltykow,³⁶ Albersloetter,² Augier and Lepoutre,⁴ Hibbs,¹⁸ and Jacobson.¹⁹

More than sixty cases of pyelitis cystica, ureteritis cystica, or cystitis cystica have been reported in the literature; cystitis cystica predominates. In many of these there were only a few cysts in the trigone of the bladder. Table I includes the most pronounced cases reported. The theories as to the cause of these conditions may be summarized as follows: (1) inflammatory closure of glands in the urinary tract; (2) inflammatory closure of crypts of the mucous membrane; (3) parasitic invasion of the urinary tract, and (4) degeneration of central epithelial cells or the secretory action of the epithelial cells of the epithelial cell nests of von Brunn.

There are likewise conflicting theories as to the formation of the epithelial cell nests of von Brunn which may be summarized thus: (1) That they are inflammatory in nature and are formed by down-

TABLE I
Marked Pyelitis, Ureteritis or Cystitis Cystica

Case	Author	Sex	Age, years	Urinary history	Urinary findings
1	Morgagni	M	60	Burning	Slight bilateral hydronephrosis and hydro-ureter. Cysts of renal pelvis and ureter (bilateral).
2	Morgagni	M	old man	Difficulty 12 years	Bilateral hydronephrosis and hydro-ureter. Right ureteral calculus; cysts of right ureter.
3	Litten	F	75		Right hydronephrosis and hydro-ureter. Right ureteral calculus; cysts of right ureter.
4	Lubarsch	M	75		Purulent pyelitis and cystitis. Dilated ureters. Vesical calculi. Cysts both ureters.
5	Lubarsch	F	78		Bilateral pyelonephritis. Ureters dilated and covered with cysts.
6	Ajutolo	F	40		Duplication of left kidney, pelvis and ureter. Lower pelvis and ureter dilated and showing cysts.
7	Ebstein	M	48	Suppuration of urinary passages; hematuria	Chronic pyelonephritis, ureteritis and cystitis. Left ureteral calculus. Cysts left renal pelvis and ureter.
8	Kahlden	F	66		Chronic interstitial nephritis with recent parenchymatous nephritis and cystitis. Cysts of upper right ureter.
9	Kahlden	M	67		Carcinoma of bladder. Cysts both ureters and renal pelvis.
10	Albersloetter	F	60		Bilateral hydronephrosis. Diverticulum of bladder with cystitis. Cysts both ureters.
11	Albersloetter	F	71		Vesical mucosa swollen and red; small blisters around neck. Cysts both ureters, especially right.
12	Liebreich	M	53	Hematuria	Ureters slightly dilated. Bladder dilated and hypertrophied. Cysts both ureters.
13	Herxheimer	M	25		Trabeculated and hypertrophied bladder. Bilateral slight hydronephrosis. Cysts both ureters.
14	Herxheimer	F	69		Pyelitis and ureteritis with necrosis of the renal papillae. Cysts of renal pelvis and ureters.
15	Augier and Lepoutre	F	86		Pyelonephritis and ureteritis. Atrophic kidneys. Left hydronephrosis and hydro-ureter; cysts left ureter.

Case	Author	Sex	Age, years	Urinary history	Urinary findings
16	Motz and Cariani	M	71		Cystitis. Cysts of trigone and fundus of bladder.
17	Motz and Cariani	M	63		Carcinoma of penis. Duplication of left ureter. Cysts of left ureters.
18	Stow	F	40		Chronic cystitis. Pyelonephritis. Complete duplication of pelvis and ureter on both sides. Numerous cysts of all four ureters.
19	Silcock	M	20		Left kidney removed. Right ureteral calculus. Cysts of bladder.
20	Voelcker	M	73		Chronic interstitial nephritis with formation of numerous cysts. Cysts left renal pelvis and ureter.
21	Hibbs	M	25		Calculus in bladder. Bilateral hydronephrosis and hydro-ureter. Cysts both pelves and ureters.
22	Harris	F	58		Death following operation for right renal calculus. Inflammation of right ureter and bladder with dilatation of ureter. Cysts right ureter.
23	Harris	M	54		Died following operation for right renal calculus. Duplication of left pelvis and ureter with calculus in upper pelvis. Cysts in ureter to upper pelvis.
24	Clark	F			Left hydronephrosis. Cysts of upper left ureter, pelvis and bladder.
25	Eve	F	51	Frequency, hematuria	Cysts both pelves and ureters.
26	Stoerk	F	57		Chronic cystitis. Cysts of both ureters.
27	Stoerk	F	60		Pyelitis, ureteritis, and hemorrhagic cystitis. Right renal stone. Cysts in ureter and trigone of bladder.
28	Jacobson	M	83	Operation; prostatic trouble 8 years before death	Duplication left pelvis and ureters to middle third. Atrophic kidneys with evidence of old pyelonephritis. Cysts both ureters and pelves on both sides.
29	Jacobson	M	74	Nocturia 15 years	Cysts of bladder.
30	Jacobson	M	66	Prostatectomy 2 years before death	Old pyelonephritis and cystitis. Cysts of ureters and pelves.

ward proliferation of the epithelium, or proliferation of the connective tissue upward between the epithelial nests to cut off islands of epithelial cells, and (2) that they are at times normally found in the urinary tract.

CASES STUDIED

One hundred twenty-five cases were observed practically consecutively at necropsy and three cases recognized macroscopically as pyelitis cystica, ureteritis cystica and cystitis cystica.

In 100 of the 125 cases, sections were taken from each renal pelvis and ureter, and from the fundus and trigone of the urinary bladder. In the remaining twenty-five cases, the renal pelvis and ureters were removed intact and mounted. Sections were taken at seven different levels, namely, renal pelvis, ureteropelvic juncture, upper, middle and lower thirds of the ureter, the fundus and trigone of the bladder.

The average age of the 125 subjects was about 44½ years, the oldest being 88 years and the youngest a fetus born in the fifth month of pregnancy.

Macroscopically, cysts were not found in the group of 125 cases. Microscopically, the so-called epithelial buds and cell nests of von Brunn or cysts were found in varying numbers and situations in 108 of the 125 cases (86.4 per cent). In Table II is a brief summary of seventeen cases in which epithelial buds, cell nests or cysts were not found.

Inflammation as judged by lymphocytic infiltration, proliferation of fibrous connective tissue, and formation of new capillaries was found in 63 (58.25 per cent) of the 108 cases showing epithelial buds, cell nests or cysts, and in four (23.6 per cent) of the cases in which no evidence of epithelial buds, cell nests or cysts were found.

In ten of the twenty-five cases in which sections were taken at seven different levels, epithelial buds, nests or cysts were found in the renal pelvis in ten cases, in the upper ureter in fifteen cases, in the lower ureter in seven cases and in the bladder in twelve cases. This confirms Aschoff's opinion that they are most common in the renal pelvis, upper portion of the ureter and bladder.

Serial sections were made at different levels in fifteen cases to establish, if possible, the presence of glands or uniform connections between the epithelial cell nests and the surface epithelium, or the presence of ducts connecting the cystic formation with the lumen of the renal pelvis, ureter or bladder. The epithelial sprouts or buds,

TABLE II

Seventeen Cases: No Epithelial Buds, Nests or Cysts

Case	Sex	Age	Inflammation	Cause of death
1	M	Full term	Absent	Still birth.
2	M	One-half hour	Absent	Prematurity (sixth month).
3	M	Eighth month	Absent	Still birth.
4	F	Six days	Absent	Prematurity (sixth month).
5	F	Three months	Absent	Cardiac anomaly.
6	F	<i>Years</i> 4	In bladder	Enucleation of right eye for neuroblastoma of the retina. Terminal bronchopneumonia.
7	F	5	Absent	Repair of right diaphragmatic hernia.
8	M	12	Absent	Glioma of the cerebellum with internal hydrocephalus.
9	F	13	Absent	Generalized peritonitis from a ruptured appendix.
10	M	18	Absent	Anterior poliomyelitis.
11	M	26	Wall infiltrated with myelocytes and other cells	Myelogenous leukemia.
12	M	38	Absent	Exploration of brain tumor. Cystic glioma of right cerebrum.
13	M	42	Slight throughout	Cholecystectomy for subacute cholecystitis with cholelithiasis. Edema of brain.
14	F	53	Absent	Cholecystectomy and appendectomy for chronic cholecystitis and appendicitis. Generalized peritonitis.
15	F	56	Subacute cystitis	Carcinoma of the ovaries with metastasis to the omentum, right ureter, and supraclavicular lymph nodes.
16	F	61	Absent	Carcinoma of the rectum with perforation and generalized peritonitis.
17	M	77	Chronic throughout	Carcinoma of the pancreas with metastasis to the liver and pleura.

as their name implies, are connected with the surface epithelium. A duct-like connection was not seen between the cystic structure and the lumen of the renal pelvis, ureter or bladder. In all cases, cysts can be seen opening on the surface. They have ruptured spontaneously or possibly in sectioning; but when the latter occurs one sees the cysts close to the surface and a good portion of the cystic envelope has disappeared.

Glands were not found in the urinary tract in the routine slides or in the serial sections, except in the trigone, where they were close to the internal sphincter of the urethra. These glands have been thoroughly studied and described by Albarran,¹ Lowsley²⁵ and others. As a rule, they are straight tubular structures lined by a double layer of cuboidal cells. Occasionally, one sees a nodule in the trigone of the bladder which somewhat resembles a cyst but which on section proves to be an encapsulated adenoma.

Egli, Litten, Hamburger and others undoubtedly saw formations which resembled glands, that is, cystic formations lined by several layers of cells, the inner layer being columnar and arranged axially.

Stoerk and Zuckerkandl⁴⁰ did not call these glands, but believed the lumen to be produced by the secretory action of the cells. Dogiel⁹ states that the surface epithelium of the urinary tract is secretory and in this Stoerk and Zuckerkandl support him in part. They state that the surface epithelium is secretory in some instances when there is increased vascularity due to inflammation, but that, whatever the secretion is, it is not mucous in character and may be only a product of degenerated epithelium. In secretions of the urinary tract, taken by catheterization and cystoscopy, they were never able to demonstrate a mucous reaction, whereas in the cystic contents there was a mucin reaction on a few occasions.

Occasionally, in these cases, I have found the surface epithelium to resemble secretory epithelium, it being columnar in type and the nuclei situated basally. In numerous specimens of the fresh cystic material, specially fixed and stained with mucin stains, I was unable to demonstrate a mucin reaction in any instance.

That the crypts of the mucous membrane may occasionally become closed off by proliferation of the fibrous tissue is easily conceivable when one sees the close proximity between the walls at the mouths of the crypts and the marked proliferation of fibrous tissue that takes place in many cases.

Those advancing the theory that these cysts are caused by parasites did so merely on the histologic appearance of certain ovoid bodies found in the cystic contents, which they maintained resembled certain coccidia. They were unable to culture these parasitic forms and, in the examination of the fresh contents of the cysts, no motile forms were found. These forms were never seen in the surrounding epithelium nor was it possible to produce the disease in animals from the contents of the cyst. Gilchrist,¹⁴ in an exhaustive study of the so-called psorospermatic diseases of the skin, has shown that degenerating epithelium gives rise to particles that simulate and have been called psorosperms. It has been established by Giani that cysts form from the epithelial cell nests of von Brunn. The method of formation of these nests is not clear. Von Brunn, Aschoff, Lubarsch, Stoerk and many others have considered them inflammatory in nature, while Giani has proved experimentally that they form as the result of inflammation. Marckwald has stated that they are occasionally normal constituents and reports a case in which they were present in a new-born child, although Herxheimer explains this by the excretion of toxic substances in the urine. Giani also states that, once the epithelial cell nests have formed, the cell nests will go on to cystic formation and eventually disappear even in the absence of the original causative factor and all signs of inflammation.

In sixty-three (58.25 per cent) of the 108 cases in which epithelial buds, cell nests or cysts were present, inflammation was manifested by lymphocytic infiltration or fibrous tissue proliferation, while in only four (23.5 per cent) of the seventeen cases remaining was there evidence of inflammation.

Fifteen of the 125 patients were under 20 years of age. In five of these fifteen cases epithelial buds, cell nests or cysts were found. Table III gives a brief summary of these cases.

It has been stated that these cysts, although inflammatory in nature, may be formed by two separate reactions of the tissue to inflammation, that is, by the proliferation of the epithelium and by the proliferation of the fibrous connective tissue. That they are formed in most cases by a combination of the two seems the most probable deduction, as they go hand in hand in inflammation of the urinary tract.

The variation in the size of the cysts is explainable on a purely

mechanical basis; that is, the size of the cyst varies with the amount and strength of the surrounding fibrous envelope, which depends, as in other conditions, on the severity and chronicity of the inflammation.

Jacobson proposed another factor in the formation of these nests: with old age and the consequent arteriosclerotic changes, the muscular walls are undernourished, and consequent muscular atrophy and atony produce excessive infolding of the mucosa, which is more

TABLE III

Five Cases Showing Epithelial Buds, Nests or Cysts (patients under twenty years of age)

Case	Sex	Age, years	Inflammation	Cause of death
1	M	5	Present	Chronic otitis media with purulent meningitis; internal hydrocephalus.
2	F	15	Present	Exophthalmic goiter. Pyelonephritis with multiple cortical abscesses.
3	M	16	Present	Cellulitis of face and neck from a furuncle. Hemorrhagic bronchopneumonia. Thrombosis left jugular vein. Multiple abscesses left kidney.
4	F	17	Present	Extensive superficial burns. Extreme emaciation. Calcium deposits both kidneys.
5	M	18	Absent	Sarcoma left leg with metastasis to lungs, liver, small intestine, and right kidney.

easily cut off into nests by proliferation of fibrous connective tissue. The formation of nests in the absence of arteriosclerotic changes he attributes to the inflammatory closure of crypts. This theory does not hold, since, in the absence of arteriosclerosis, definite epithelial budding and nest formation have been demonstrated.

In these cases the mucosa of the urinary tract reacted in four separate ways or in any combination of these four: (1) by desquamation of its epithelium, as seen in acute inflammatory processes; (2) by a papillary overgrowth or, as it is sometimes called, villous cystitis; (3) by proliferation of the lower layer of the epithelium with the formation of epithelial buds or sprouts; and (4) by cornification of the epithelium or, as it is commonly known, leukoplakia.

ILLUSTRATIVE CASES

CASE 1. A woman, aged 46, complained of a mass in the left lower portion of the abdomen. Eight years before, a ventral hernia had been repaired, and one year following this an operation was performed for intestinal adhesions. During the last two years, she had had attacks of crampy abdominal pain, which occurred two to three times a week and were associated with severe constipation. There was no history of urinary symptoms.

There was an incarcerated left inguinal hernia and a small umbilical hernia. The urine contained ten pus cells to a high power field. At operation these hernias were repaired and at that time cholecystitis and cholelithiasis were found. Fourteen days later, cholecystectomy was performed. Three days afterward the patient died.

At necropsy a left-sided subdiaphragmatic abscess and myocarditis were found, as well as acute nephritis implanted on chronic nephritis. The left renal pelvis and ureter on both sides showed isolated, bleb-like cysts up to 4 mm. in diameter, which contained a slightly brownish, gelatinous or sago-like substance (Fig. 1). Cysts were not found in the bladder.

CASE 2. A woman, aged 76, complained of dizziness associated with numbness of the right forearm and hand for the previous six months. The peripheral arteries showed marked sclerosis. The cardiac dullness was increased. The systolic blood pressure was 194 and the diastolic 86. There was definite weakness of the muscles of the right hand and forearm. The specific gravity of the urine was 1.014; it was alkaline and gave a definite reaction for albumin. Microscopically, there were from one to fifteen pus cells in each high power field. The patient died four days after admission.

At necropsy acute nephritis superimposed on chronic nephritis, myocarditis with coronary sclerosis, chronic vegetative aortic and mitral endocarditis, general arteriosclerosis, chronic catarrhal cholecystitis and cholelithiasis and left nephrolithiasis were found. The left renal pelvis and ureter showed several translucent cyst-like formations, some of which appeared pedunculated and contained a yellowish gelatinous material (Fig. 2).

CASE 3. A man, aged 64, complained of a general breakdown one year previously. At the time of this breakdown he was considerably

improved by treatment in a hospital for a month. The breakdown was characterized by dyspnea and edema of the lower extremities, both of which returned after dismissal from the hospital. In the year there had been a gradual increase in the severity of these symptoms and mental failure had progressed.

The patient was emaciated and dyspneic and came in a wheelchair. The right side of his face was flaccid and the tongue protruded to the left. The peripheral arteries were markedly sclerosed. The systolic blood pressure was 170 and the diastolic 110. The apex beat was diffuse and considerably to the left; a blowing systolic murmur was heard best over the pulmonic area. There was marked edema of the lower extremities. The urine was acid and its specific gravity 1.007; there was marked reaction for albumin. There were numerous granular and hyaline casts and from thirty to fifty pus cells in each high power field. The blood urea was 456 mg. for each 100 cc. Death ensued eighteen days after admission.

Necropsy showed marked generalized arteriosclerosis, cardiac hypertrophy and dilatation, atrophy and scarring of the kidneys, and multiple cortical cysts following old healed pyelonephritis. Both the renal pelvis and ureter on each side showed isolated cyst-like structures. Chronic cystitis was present, and the trigone showed multiple cyst-like formations (Fig. 3).

DISCUSSION OF CASES

Microscopic sections in these cases showed numerous epithelial cell nests and cysts in all stages of development associated with a diffuse inflammatory process. The lumen was filled with a colloid-like material in which red blood corpuscles and degenerated epithelial cells were seen. The lining of these macroscopic cysts, as a rule, consisted of a single or double layer of flat epithelial cells, resembling somewhat endothelial cells, surrounded by a dense fibrous tissue envelope.

It is rather hard to understand why epithelial cell nests and microscopic cysts are common while macroscopic cysts are so seldom found at necropsy. In a cystoscopic experience of any extent, it is rather common to find cysts of the mucosa of the bladder in cases of long-standing inflammatory disease. In the examination of the records of 190 cases of bilateral pyelonephritis, cystitis cystica was found in

thirty-three (17.4 per cent). The cysts are usually found in the trigone and base of the bladder but are occasionally diffusely scattered over the remainder of the mucosa.

This seemingly conflicting evidence is probably in part due to the fact that, unless carefully searched for, the smaller cysts are easily overlooked, particularly in the presence of marked inflammatory reaction.

CONCLUSIONS

1. Glandular structures are not normally found in the urinary tract above the trigone of the bladder.
2. Epithelial buds, cell nests, and cysts are not normally found in the urinary tract.
3. Cysts of the urinary tract are formed from the epithelial nests of von Brunn.
4. The epithelial buds and cell nests of von Brunn are inflammatory in nature.
5. Microscopically, epithelial buds, cell nests and cysts are present in the majority of persons more than 20 years of age.
6. This study does not reveal evidence to support the secretory theory of the formation of these cysts.
7. The cysts are formed by degeneration of the central cells of the epithelial cell nests.

REFERENCES

1. Albarran, Joaquin. *Maladies de la Prostate*. 1902, 526.
2. Albersloetter, H. Über die Pathogenese der Ureteritis cystica. *Müncher*, 1909.
3. Aschoff, Ludwig. Ein Beitrag zur normalen und pathologischen Anatomie der Schleimhaut der Harnwege und ihrer drüsigen Anhänge. *Virchows Arch. f. path. Anat.*, 1894, cxxxviii, 119.
4. Augier, D., and Lepoutre, C. Étude d'un cas d'urétérite kystique. *Ann. d. mal. d. org. génito-urin.*, 1911, xxix, 880.
5. Bland-Sutton, J. Psorospermiae in ureter. *Brit. M. J.*, 1889, ii, 1392. On parasiticism by psorospermia. *Lancet*, 1889, ii, 1278.
6. von Brunn, A. Über drüsenähnliche Bildungen in der Schleimhaut des Nierenbeckens des Ureters und der Harnblase beim Menschen. *Arch. f. mikr. Anat.*, 1893, xli, 294.
7. Clark, J. J. Mucous cysts of ureter. *Brit. M. J.*, 1892, i, 274.
A case of psorospermial cysts of the left kidney and ureter, and of the bladder, with hydronephrosis of the left kidney. *Tr. Path. Soc. London*, 1892, xliii, 94.

8. D'Ajutolo, D. G. Ueber Uretheritis chronica cystica. *Centralbl. f. allg. Pathol. u. path. Anat.*, 1890, i, 266.
9. Dogiel, A. S. Zur frage über das Epithel der Harnblase. *Arch. f. mikr. Anat.*, 1890, xxxv, 389.
10. Ebstein, W. Zur Lehre von den chronischen Katarrhen der Schleimhaut der Harnwege und der Cystenbildung in derselben. *Deutsches Arch. f. klin. Med.*, 1882, xxxi, 63.
11. Egli, T. Ueber die Drüsen des Nierenbeckens. *Arch. f. mikr. Anat.*, 1873, ix, 653.
12. Eve, F. S. Psorospermial cysts of both ureters. *Tr. Path. Soc. London*, 1889, xl, 444.
13. Giani, R. Neuer experimentellen Beitrage zur Entstehung der Cystitis cystica. *Beitr. z. path. Anat. u. z. allg. Pathol.*, 1907, xlii, 1.
14. Gilchrist, T. C. The so-called protozoa occuring in psorospermiosis follicularis vegetans (Darier). *Rep. Johns Hopkins Hosp.*, 1896, i, 291.
15. Hamburger, A. O. Zur Histologie des Nierenbeckens und des Harnleiters. *Arch. f. mikr. Anat.*, 1879, xvii, 14.
16. Harris, H. Cysts of the ureter. *Am. Med.*, 1902, iii, 731.
17. Herxheimer, Gotthold. Ueber Cystenbildungen der Niere und abführenden Harnwege. *Virchows Arch. f. path. Anat.*, 1906, clxxxv, 52.
18. Hibbs, W. G. Hyperplastic pyelitis and ureteritis cystica. *Tr. Chicago Path. Soc.*, 1919, xi, 49.
19. Jacobson, V. C. Pyelitis et ureteritis et cystitis cystica. *Bull. Johns Hopkins Hosp.*, 1920, xxxi, 122.
20. Johnson. Quoted by Jacobson.
21. von Kahlden, C. Ueber Ureteritis cystica. *Beitr. z. path. Anat. u. z. allg. Pathol.*, 1895, xvii, 562.
22. Liebreich, A. Ein Fall von Ureteritis cystica. Tübingen, 1906.
23. von Limbeck, R. Zur Kenntniss der Epithelcysten der Harnblase und der Ureteren. *Ztschr. f. Heilk.*, 1887, viii, 55.
24. Litten, M. Ureteritis chronica cystica polyposa nebst cystischer, Degeneration der Niere. *Virchows Arch. f. path. Anat.*, 1876, lxvi, 139.
25. Lowsley, O. S. Observations on certain obstructions at the vesical orifice. *J. A. M. A.*, 1917, lxxviii, 444.
26. Lubarsch, O. Ueber Cysten der ableitenden Harnwege. *Arch. f. mikr. Anat.*, 1893, xli, 303.
27. Marckwald. Die multiple Cystenbildung in den Ureteren und der Harnblase, sog. Ureteritis cystica. *München. med. Wchnschr.*, 1898, xlv, 1049.
28. Morgagni, J. B. De sedibus et causis morborum per anatomen indagatis libri quinque. William Cooke Translation, London, 1822, ii, 316, 411.
29. Morris, H. Surgical Diseases of the Kidney and Ureter. London, 1901, ii, 480.
30. Motz, B., and Cariani, A. Contribution à l'étude des adénomes kystiques de l'appareil urinaire. *Ann. d. mal. d. org. genito-urin.*, 1904, xxii, 1305.
31. Osler, William. Psorospermiasis. The Principles and Practice of Medicine. New York, 1920, Ed. 9, 336.

32. Pisenti, G. Ueber die parasitische Natur der Ureteritis chronica cystica. *Centralbl. f. allg. Pathol. u. path. Anat.*, 1894, v, 657.
33. Radtke, Erich. Beiträge zur Kenntniss der Ureteritis cystica. Königsberg, 1900.
34. Rayer, P. F. *Traité des Maladies des Reins*. Paris, 1837, Atlas, Plate lii, Figs. 2, 3, and 4.
35. Rokitsansky, Carl. *Manual of Pathological Anatomy*. London, 1861, Ed. 2, 216.
36. Saltykow, S. Epithelveränderungen der ableitenden Harnwege bei Entzündung. *Beitr. z. path. Anat. u. z. allg. Pathol.*, 1908, xliv, 393.
37. Satani, Y. Histologic study of the ureter. *Urol.*, 1919, iii, 247.
38. Silcock, A. Q. Case of vesiculation of the mucous membrane of the bladder. *Tr. Pathol. Soc. London*, 1888-1889, xl, 175.
39. Stoerk, Oskar. Beiträge zur Pathologie der Schleimhaut der harnleitenden Wege. *Beitr. z. path. Anat. u. z. allg. Pathol.*, 1899, xxvi, 367.
40. Stoerk, O., and Zuckerkandl, O. Ueber Cystitis glandularis und den Drüsenkrebs der Harnblase. *Ztschr. f. Urol.*, 1907, i, 3, 133.
41. Stow, B. Ureteritis cystica chronica. *Ann. Surg.*, 1907, xlvi, 233.
42. Voelcker, Arthur. Chronic interstitial nephritis with cysts in the renal pelvis, double ureter and malformation of the bladder. *Tr. Path. Soc. London*, 1898, xlix, 168.
43. Virchow, Rudolph. *Die krankhaften Geschwülste*. Berlin, 1863, Ed. 1, 246.

DESCRIPTION OF PLATE

PLATE 15

- FIG. 1.** Case 1. Left kidney and ureter. Cysts of the renal pelvis and ureter.
- FIG. 2.** Case 2. Left kidney and upper ureter. Calculus in upper calyx and cysts in the renal pelvis and ureter.

1

Morse

2

Pyelitis, Ureteritis and Cystitis Cystica

PLATE 16

FIG. 3. Case 3. Kidneys, ureter and bladder; cysts of the renal pelvis, ureters and trigone of the bladder.