

POLYCYSTIC DISEASE OF THE KIDNEY

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POLYCYSTIC kidney disease is of more than passing interest to both the clinician and the surgeon. In the first place, while not a common condition, it is by no means rare. In collected statistics of 23,900 autopsies, sixty-seven cases of bilateral polycystic kidneys were found.¹ In a local hospital, thirteen cases occurred in 2,060 autopsies.² In our series, there were sixty proved cases in 220,000 admissions, a ratio of 1:3,500, and out of a total of 6,000 necropsies, fourteen cases were encountered or a ratio of 1:428. The Mayo Clinic had an incidence of 1:3,523 in 680,000 registrations and of 1:1,019 in 9,171 autopsies.³ In any fairly large hospital, three or four of these cases will be seen each year.

From a practical viewpoint, the methods of diagnosis are important. While often the picture is typical, there are times when a differential diagnosis must be made from malignant neoplasm, bilateral hydronephrosis, pyonephrosis, calculous disease of the kidney, and chronic cardiovascular renal disease.

The pathogenesis of polycystic disease of the kidney has been the subject of many investigations, but in spite of a large amount of research, none of the theories of etiology completely explains all the pathological and experimental data. Moreover, the operative indications for its treatment have not been standardized, and should be reevaluated in the light of present knowledge and past experience.

Polycystic kidney disease should be defined in contrast to other cystic conditions of the kidney whether single, multiple, or multilocular. Small epithelial-lined cavities are found in kidneys at all age periods.⁴ According to Lubarsch,⁴ they increase numerically with age. In the newborn and up to one and a half years of age, more than 50 per cent. of kidneys show such cysts according to Rückert,⁵ Herxheimer,⁶ and Braunwarth.⁷ The dividing line between simple cysts and polycystic disease is not clear cut. Thus, the microscopical appearance of a single cyst from a polycystic kidney may present the same features as one of the multiple cysts found in arteriosclerotic kidneys. For example, both types may have thin walls surrounded by compressed, fibrosed kidney tissue and lined by a layer of flattened epithelial cells. A kidney may be considered "polycystic" when there is an excessive number of small and larger cysts found throughout its parenchyma and projecting on its surface. Both cortex and medulla are involved; sometimes one more than the other. There may be a large amount of fairly normal parenchyma left or there may be complete gross absence of renal tissue depending on the stage reached. While there may be some evidence to explain most types of cysts on a con-

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genital basis (see Orth⁸ and Kampmeier⁹), in this study only kidneys which have the gross characteristics above described are considered truly congenital polycystic. These alone are associated with other well-known characteristics such as familial and hereditary tendencies, bilaterality of occurrence, and the symptom complexes to be described below. The consideration that a gross pathological diagnosis of polycystic kidney depends upon the excessive degree of cystic involvement is important, too, in the evaluation of unilateral cases. When one kidney is grossly polycystic, the presence of occasional cysts of microscopical size in the opposite kidney would not compel a diagnosis of bilateral polycystic kidney since such occasional cysts are often found in otherwise normal kidneys. If, however, such a kidney shows a really extreme number of small or microscopical cysts such as would undoubtedly go on to the formation of a grossly polycystic kidney as already apparent in the opposite kidney, the diagnosis of bilateral polycystic kidney is justified.

This study is based on sixty cases observed between the years 1911 and 1932. Six were from the office of Dr. Edwin Beer and fifty-four were admitted to the Mount Sinai Hospital, New York City. Fourteen of these patients came to post-mortem examination.

Polycystic kidney disease is known clinically in two forms, *i.e.*, in the newborn and in adults. The former is seen more often in the lying-in hospitals and is frequently associated with various other congenital anomalies, some of which may be incompatible with life. These anomalies run the whole gamut of developmental imperfections such as hare-lip, cleft palate, hypospadias, rudimentary external genitalia, vesico-rectal fistulæ, bladder malformations, atresia of the vagina or rectum, imperforate anus, malformations of the sigmoid, cardiac malformations, uterine aplasia, polydactylism, club feet, meningocele, hydrocephalus, spina bifida, and porencephaly.^{1, 5, 10, 11, 12} While anomalies occasionally occur in the adult cases, they are not common. No malformations were noted in this series.

Cases of dystocia due to cystic kidneys are well known and of importance to the obstetrician. In fact, the earliest described cases of polycystic kidney were those encountered as a cause of obstructed labor reported by Alexis Littre¹³ around 1700 and by Othmar Heer¹⁴ and by Osiander.¹⁵ Almost yearly such case reports occur in the literature.^{17, 18, 19, 20}

Many of the newborn cases die at birth or shortly after. The rest are unrecognized and reach adult life before presenting signs and symptoms of their condition. A few infants, however, live to develop symptoms or die of intercurrent disease before the age of two or three. In such instances the syndrome of renal rickets or renal dwarfism may be present, as seen also in chronic nephritis, with bone changes and disturbances in the calcium and phosphorus ratio in the blood. (Mitchell,²¹ Green.²²)

There is only one newborn case in this series, a six-month-old female child, admitted to Doctor Schick's service, with clinical signs of nasopharyngitis and pneumonia. She had been born as a seven months' premature infant. Death occurred after a nine-day illness, and post-mortem showed bilateral

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polycystic kidneys, each the size of a hen's egg, hypertrophy of the left ventricle and fatty infiltration of the liver. Three other infants had been born to the same mother and had died, one at seven days, one at two days, and one a stillbirth in the seventh month of gestation. Since there was no evidence of lues, the possibility must be considered that the other infants had congenital malformations, in particular, polycystic kidneys.

The remaining fifty-nine patients were of the adult type. The following data are based on their study.

Sex.—Thirty-seven patients were males and twenty-two were females.

Age Groups.—The age groups are seen in Table I.

TABLE I

Years	No. of Patients
1-9	0
10-19.....	0
20-29.....	2
30-39.....	14
40-49.....	17
50-59.....	18
60-69.....	8

These represent the age when the patient first came under observation. It should be noted that the great majority of cases on admission were between the ages of thirty-five and fifty-five. The average age of the patients at the onset of their symptoms was calculated as being 41.5 years. From this table, there is evident a wide age gap between the newborn and infant cases and the adult cases. This had been known to Virchow²³ who, however, was unable to explain it. This occurrence is the basis of the contention on the part of some observers that the newborn and the adult forms represent different diseases.

It is our belief that the tremendous margin of safety present in the kidneys explains the fact that cases remain symptomless during the first two decades of life. In our own series a female patient, first seen by us at the age of thirty-seven, had had a nephrectomy for polycystic kidney at another hospital

TABLE II

Stillborn or dying shortly after birth....	59
Died in 1st year life.....	10
1-5	6
5-10.....	1
10-20.....	4
20-30.....	22
30-40.....	24
40-50.....	53
50-60.....	41
60-70.....	10
70-80.....	6
80-90.....	3

Total 239

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at the age of twenty-three. Undoubtedly, she must have had the condition for a number of years previous to this. Another female patient had symptoms which started at twenty-six. She was first observed at twenty-eight and finally died in this institution in uræmia at the age of forty.

Küster²⁴ has published an interesting table of age groups of collected cases from the literature which some recent authors have erroneously attributed to Stromberg. (See Table II.)

Particularly important are the cases between two and twenty. Küster found the following cases:

TABLE II

	Years
Park.....	2
Hildebrand.....	2
Graser.....	2½
Ore.....	2½
Talamon.....	5
Orth.....	14
Harris.....	18
Beckmann.....	19
Höhne.....	20
Johnson.....	20
Gairdner.....	18
Israel.....	15*

* This patient died at twenty-five with symptoms of ten or fifteen years' duration.

From Albarran and Imbert,²⁵ Sieber²⁶ quotes the following cases:

	Years
Jacobson.....	2½
Steiner.....	10
Steiner.....	10
Heimann.....	11
Lucet.....	17
Edmunds.....	18
Bar.....	19

Sieber²⁶ found the following additional cases:

	Years
Meyer.....	2
Meyer.....	6
Meyer.....	9
Türk.....	17
Richmond.....	18

A casual search of the recent literature reveals the following cases:

Willan²⁷ 17—female died in uræmia at 31, known to have a kidney tumor when a few months old; symptomless until age of 17.

Rossen²⁸ 9—at onset of symptoms—died at 14.

Cumming²⁹ 14—at death—treated for nephritis since 6 years old.

Halbertsma³⁰ 10—girl with unilateral mass, hypertension, typical pyelogram, hæmaturia, whose father had the same condition.

Schapiro³¹ 10—boy who was examined at 10 for polycystic kidneys because of a pronounced familial history. At 13 had a trace of albumin in his urine. Rejected for life insurance at 19 years at which time both kidneys were enlarged and nodular.

The occurrence of these twenty-nine cases between the ages of two and twenty would seem to be a connecting link between the newborn and adult types of the same disease.

Mortality and Follow-up.—Twenty-six of the fifty-nine patients or approximately 43 per cent. are known to be dead. The average age at death was fifty years. The earliest death was at twenty-six years while the latest age at death was sixty-eight. In general, then, these individuals have a life expectancy of about ten or twelve years less than that of the average individual. Of the living patients, seven have been followed regularly to the present time, while the remaining twenty-six cases, although followed for varying periods of time, have an incomplete follow-up record. The total duration of the patients' symptoms, calculated from the history and time under observation until the last follow-up date or until death, is given in Table III under these headings, *viz.*: for the cases that died, for those with a partial follow-up, and for those with a complete follow-up.

TABLE III

Duration of Symptoms	Number of Cases		
	Died	Partial F.U.	Complete F.U.
Less than 1 yr.	3	6	0
1 yr.	1	4	0
2 yrs.	6	3	1
3 yrs.	3	2	0
4 yrs.	1	1	2
5 yrs.	2	1	2
6 yrs.	2	1	1
7 yrs.	1	3	0
8 yrs.	1	0	1
9 yrs.	0	1	0
10 yrs.	2	1	0
12 yrs.	1	1	0
13 yrs.	1	0	0
14 yrs.	1	2	0
19 yrs.	1	0	0
Total.	26	26	7

The tendency to chronicity and long duration of symptoms is well illustrated. Ten cases had symptomatic evidences of their condition for ten years or more.

Familial and Hereditary Factors.—The frequent occurrence of multiple cases of polycystic kidney in the same family is well known. This hereditary predisposition appears to be equally transmitted by either sex. The literature is replete with such reports, the most remarkable being that of Crawford³² who found seventeen cases in a family of forty members. Dunger,³³ Bull,³⁴ Borelius,³⁵ Osler,³⁶ Bunting,³⁷ Wobus,³⁸ Cumming,²⁹ and many others have

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confirmed this hereditary tendency which, together with the frequency of occurrence of newborn cases and of other congenital anomalies, proves the congenital nature of the disease. In this series there were eight cases (about 14 per cent.) with a proved familial history of polycystic kidney disease. Of these, two were brothers, and three were father, son and daughter. The sixth patient had a brother who died of the condition, the seventh had an aunt who died of it, while the eighth had a sister who died at another hospital following a nephrectomy for polycystic kidney. Besides these eight patients there were three others with a probable but not proved familial history.

Unilateral Polycystic Kidney.—There were no proved unilateral cases in this group. For practical purposes every case of polycystic kidney may be considered bilateral. However, the incidence of the unilateral form of the disease in different series varies considerably. Lejars³⁹ found three unilateral cases in sixty-two cases. Ritchie⁴⁰ found two in eighty-eight cases autopsied. Naumann⁴¹ found two unilateral and fourteen bilateral cases in 10,177 necropsies. Bugbee and Wollstein¹² found four unilateral and eleven bilateral cases in 4,903 necropsies in infants. Dickinson⁴² thought the ratio was about 1:26 while Luzzato⁴³ believed that 18.1 per cent. of the cases were unilateral.

Undoubtedly some of the statistics based on clinical data are not entirely accurate. Simple palpation at operation alone cannot be relied upon for proof that the non-nephrectomized kidney is normal, despite clinical reports to the contrary⁴⁴. It is an important surgical fact that when nephrectomy has been done for polycystic kidney in a case in which the second kidney had appeared normal to the surgeon's palpating hand, the latter kidney is very likely to become polycystic subsequent to the operation. Reimann⁴⁵ saw three such cases. Barnett⁴⁶ changed his earlier views on unilateral cases; one of his cases reported originally as unilateral which had been subjected to nephrectomy, developed five years later signs of involvement of the remaining kidney with anuria. Of nine patients diagnosed as having unilateral disease in 1912, Barnett found that five developed polycystic changes in the other kidney by 1917.

It is probable that in some of the cases included in the post-mortem statistics quoted above concerning unilateral polycystic disease, complete microscopical study of the grossly uninvolved kidney was not done. Undoubtedly, as Barnett claims, many more cases would show microscopical cysts in sufficient number to be included with the cases of bilateral disease than such statistics would indicate. In conformity with this is the viewpoint expressed by Braasch and Schacht³ who state that "polycystic kidney is always bilateral in the adult." Nevertheless undoubted cases of unilateral cystic disease must exist as in the following two cases which were very kindly placed at my disposal by Dr. Max Lederer, pathologist to the Brooklyn Jewish Hospital. At that institution there were two unilateral cases and eleven bilateral cases found in 2,060 autopsies.

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CASE I.—Italian male, 60 years of age. Admitted December 3, 1925, and died shortly after admission. He had had headaches, vertigo, and spots before the eyes for six months. Suddenly had an attack of apoplexy with unconsciousness. Became cyanotic with Cheyne-Stokes respirations and pulmonary œdema. He had a right hemiplegia. Blood-pressure 230/140. Phlebotomy and spinal tap performed.

Post-mortem.—Obese; heart enlarged, ventricular hypertrophy and dilatation; patent foramen ovale. Liver—no cysts.

Kidneys.—(Left.) Typical appearance of polycystic kidney (Fig. 1); was about twice the size of the right kidney, containing multiple cysts of varying sizes; only a portion of its upper pole was uninvolved. *Microscopically.*—The cysts showed the usual appearance.

(Right.) Contained no cysts; weighed 256 Gm.; many depressed areas on the surface.

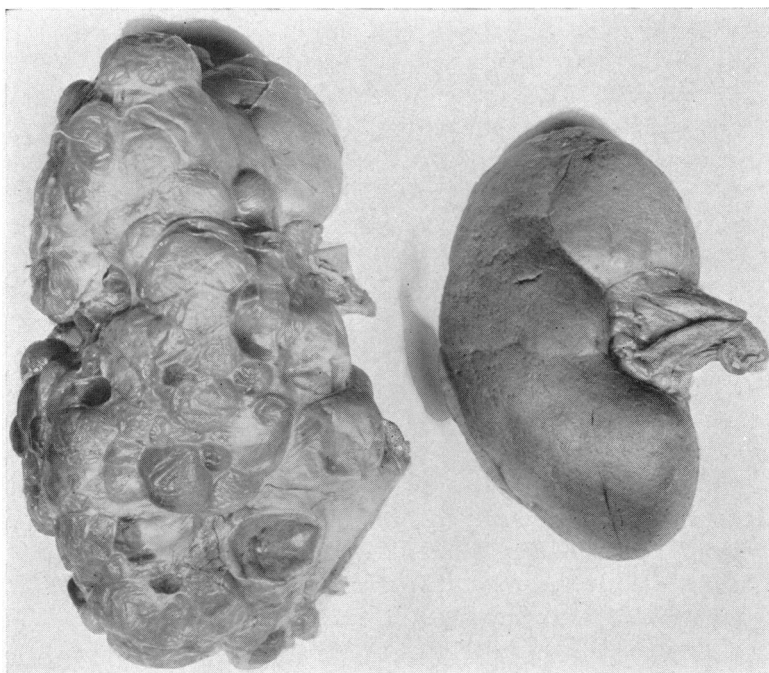


FIG. 1.—Unilateral left polycystic kidney. (Specimen in fixative for eight years.)

Microscopically.—œdema and congestion involving glomeruli; smaller vessels sclerotic with associated areas of round-cell infiltration and focal fibrosis. An occasional small lacuna lined by flattened epithelium. The brain showed a cerebellar hæmorrhage.

Pathological Diagnosis.—Cerebellar hæmorrhage and cerebral arteriosclerosis. Generalized arteriosclerosis. Focal nephrosclerosis. Parenchymatous degeneration of the liver. Unilateral polycystic kidney.

CASE II.—Full-term, white, male newborn child, spontaneously delivered March 14, 1933. An imperforate anus was present for which a perineal incision and exploration for the rectum was performed. The rectum was not found and a left-sided colostomy was done. The sigmoid could not be brought to the perineum and was sutured to the abdomen. The infant expired eight hours post-operation.

Post-mortem.—The rectum was reduced to a fibrous cord for a distance of six centimetres and was fixed to the tip of the coccyx. The liver was normal.

Kidneys.—(Right.) Small, consisted almost in its entirety of numerous cysts con-

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taining clear fluid; no renal tissue discernible. *Microscopically*.—It showed the picture of a polycystic kidney; there were individual normal groups of kidney parenchyma with well-preserved tubules and glomeruli, isolated by fibroplastic interstitial tissue which often appeared embryonal in character; many tubules dilated in cyst-like formation with flattened lining epithelium; larger and smaller cysts.

(Left.) Was increased in size over the normal; uric acid crystals present in the apices of the pyramids but otherwise it was normal. *Microscopically*.—Kidney appeared normal; no cysts present.

Pathological Diagnosis.—Atresia of the rectum with imperforate anus. Unilateral polycystic kidney. Pulmonary infarction. Bronchopneumonia. Incomplete spina bifida. Patent ductus arteriosus and foramen ovale.

Clinical picture on admission—Modes of onset or discovery.—The cases grouped themselves into eight main clinical forms as follows:

- (1) Accidental discovery, as at operation, post-mortem examination or the findings of a symptomless mass in the abdomen 6 cases.
- (2) Symptoms and signs of hypertensive cardiorenal disease. Malignant hypertension, primary arteriosclerosis, and the later stages of chronic glomerular nephritis may give the same picture as the disease under consideration 13 cases.
- (3) Symptoms and signs resembling those of renal neoplasm, namely, unilateral mass, pain, and hæmaturia 7 cases.
Of these the diagnosis in four cases was made by an exploratory lumbar incision.
- (4) Symptoms and signs suggestive of infected hydronephrosis, pyelonephritis or perinephric abscess 3 cases.
- (5) Cases with vague abdominal symptoms as abdominal pains, vomiting, eructations, constipation, and distention 5 cases.
- (6) Frank symptoms and signs of polycystic kidney, namely, hæmaturia, loin pain, bilateral loin masses, arterial hypertension, and evidences of renal insufficiency 15 cases.
- (7) Case with acute retroperitoneal syndrome 1 case.
An unusual case to be described later.
- (8) Symptoms, signs and X-ray evidence of renal calculi 9 cases.

Points in history. Symptoms presented on admission or occurring during period of observation of the patient:

	Number of Patients		Number of Patients
Loin pain	28	Anorexia	8
Abdominal pain	21	Weakness	8
Hæmaturia	21	Dysuria	7
Nocturia	19	Fever	7
Loss in weight	18	Dizziness	7
Vomiting	14	History of hypertension	7
Tumor mass	13	Cough	6
Dyspnœa	12	Polyuria	5
Frequency of urination	11	Edema	5
Headache	9	Constipation	5
Pyuria	8	Previous kidney trouble	5
Nausea	8	Oliguria	5

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Polydipsia	4	Paræsthesias	2
Apoplectic stroke	4	Frequent colds	2
Previous operations for poly- cystic kidney	4	Drowsiness	2
Previous abdominal operation not for polycystic kidney	4	Gain in weight	2
Abdominal distention	2	Restlessness	1
		Echymoses	1

Physical Signs—

Kidneys:

Both kidneys palpable and enlarged	39 (66 per cent.)
Right kidney only, palpated	4
Left kidney only, palpated	6
Neither kidney palpated	10

Of the last, four were cases which were discovered at post-mortem examination. The typical palpatory finding in a polycystic kidney is that of a firm, hard, nodular mass located in the loin or upper quadrant of the abdomen, which moves on respiration and which is distinctly ballottable.

Liver.—An enlarged, palpable liver was present in fifteen cases (25.4 per cent.). This enlargement had no relation to cystic involvement but was found to be due to parenchymatous or fatty degeneration, or to chronic passive congestion in those cases which showed cardiac weakness.

Heart.—An enlarged heart was present in nineteen cases (30.5 per cent.) as judged by physical examination, X-ray or post-mortem studies.

Vascular system.—Signs of peripheral arteriosclerosis were present in fourteen cases (23.7 per cent.).

Fundi.—There were ocular fundus changes in twelve cases. Many of the earlier cases did not have routine eye examinations, so that an estimate of the frequency of these changes in our cases is of no value. However, recent observers⁸ found ocular abnormalities in 57 per cent. of their cases. In our series the changes were mainly vascular, *viz.*, angiosclerotic in nature, with occasional retinitis or hæmorrhagic retinitis.

Laboratory Data—

Urinary Findings. 42 cases (71 per cent.) showed from a trace to four plus albumin. 10 cases had casts in the urine. 30 cases were uninfected as judged by the urinary findings. 10 cases showed from occasional to many white blood cells. 19 cases (32 per cent.) showed clumped white blood cells to large quantities of pus in the urine.

Red blood cells were present in the urine at one time or another in 33 cases (56 per cent.). The frequency of red blood cells in the urine is easily understood according to Ritter and Baehr.⁴⁷ They state that while hæmaturia and hæmorrhage into cysts are not necessarily dependent on arterial hypertension, their likelihood is increased by its presence. By means of arterial injections they showed how the interlobar and interlobular arteries lie in the cyst walls. In the larger cysts there are numerous arteries of various sizes beneath the lining epithelium. As the cysts increase in size, the arteries do not stretch in proportion and come to lie in the cyst cavity in a falciform fold of lining epithelium, lying unsupported. Slight trauma, local vascular disease, and hypertension may easily cause hæmorrhage into cysts with lumbar pain and possible secondary rupture into a calyx with hæmaturia. Undoubtedly, in many instances the hæmaturia is due to venous stasis and congestion involving the pelvis and peripelvic tissues. The bleeding may result from direct rupture or from brisk diapedesis.

Tests of kidney function.—The concentration test (Volhard) showed a fixation of specific gravity at or below 1012 or 1014 in seventeen cases out of twenty-eight (61 per cent.).

Phenolsulphonphthalein Test.—This test was unrecorded in twenty-five cases. Out of thirty-four cases, the output in four hours was greater than 50 per cent. in seven. In

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eleven cases it was between 10 and 40 per cent. In ten cases it was less than 10 per cent. while six cases had a zero output. In other words, twenty-seven out of thirty-four tested cases (79 per cent.) showed renal impairment by this method.

Blood Urea Nitrogen.—This was recorded in forty-five cases, as follows :

Under 20 milligrams per 100 cubic centimetres	12 cases
20 to 50 milligrams per 100 cubic centimetres	13 cases
51 to 100 milligrams per 100 cubic centimetres	4 cases
Over 100 milligrams per 100 cubic centimetres	16 cases

The highest was 190 milligrams. Thirty-three cases showed an elevated urea nitrogen at one time or another (73 per cent.).

As judged by laboratory tests alone, 71 per cent. of the patients, while under observation, showed evidences of renal impairment.

Blood-pressure.—The following figures represent the highest systolic readings in any case while under observation :

200 (or above) millimetres mercury	13 cases
160 to 200 millimetres mercury	16 cases
140 to 160 millimetres mercury	9 cases
120 to 140 millimetres mercury	5 cases
100 to 120 millimetres mercury	6 cases
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Total	49 cases
Not charted	10 cases

The highest reading was 272/112. In relation to their age, twenty-eight cases (57 per cent.) showed hypertension while twenty-one cases did not. Twenty-two cases had a diastolic pressure of 100 or above.

Braasch⁴⁸ and Schacht⁴⁹ among others have commented on the frequency of significant persistent hypertension in these cases. They attribute the hypertension to a generalized vascular disturbance as shown by the high incidence of retinal sclerosis and to the findings of obliterative changes in the arterioles and small arteries of the kidneys. Hinman and Morrison,⁵⁰ and Ritter and Baehr⁴⁷ have demonstrated these renal vascular changes by their injection studies. Whether the vascular sclerosis, especially in the kidneys, is the primary factor, and the hypertension and renal functional disturbance secondary is a moot point.

Experiments in animals, producing varying reductions of the total renal substance, while not conclusive, have shed some light on the subject. Pässler and Heinecke⁵¹ and Chanutin and Ferris⁵² found that where a chronic state of renal insufficiency was thus produced, hypertension and cardiac hypertrophy resulted without vascular sclerosis. Cash⁵³ noted that where the total kidney mass was reduced by one-half (by nephrectomy), ligation of the blood supply to a portion of the remaining kidney was followed by an increased systolic and diastolic blood-pressure. In polycystic kidneys where the total functioning renal substance is so grossly reduced, it is conceivable that pressure effects on vessels may create a situation such as was produced experimentally by Cash with a resultant hypertension. The latter in turn would lead to a secondary vascular sclerosis.

The correlation between the blood-pressure and renal function in this series was more closely analyzed as follows :

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Of 21 cases *without* hypertension in relation to age

- In 11 the kidney function was normal
- In 2 the kidney function was slightly impaired
- In 8 the kidney function was poor

Of the latter eight cases, four had evidences of cardiac failure, one had bronchopneumonia and one was in collapse. Some of these cases had a history of preëxisting hypertension. Only two cases, then, with marked impairment of kidney function and without other complicating factors had normal blood-pressures.

Of 28 cases *with* hypertension

- In 20 the kidney function was poor.
- In 2 the data were incomplete on kidney function.
- In 3 the kidney function was fair, *i.e.*, although there was no clinical evidence, there was laboratory evidence of beginning impairment, *e.g.*, normal blood chemistry and phenolsulphonphthalein output with diminution of concentrating power or perhaps urea nitrogen at upper limit of normal with moderate diminution of the phenolsulphonphthalein output.
- In 3 the kidney function was normal. Of the latter group, one case while still under observation, showed beginning impairment of function.

The following three cases are illustrative of discrepancies which occur in attempts to generalize concerning the behavior of the blood-pressure in relation to renal function:

CASE III.—Female patient; when first seen had slight elevation of blood-pressure with normal renal function. Twelve years later, had high blood-pressure with definite renal impairment. Here the hypertension preceded the impaired kidney function.

CASE IV.—Female patient who had a normal blood-pressure with slight kidney insufficiency. Four years later had a severe hypertension with moderate kidney insufficiency, or impaired renal function preceded the hypertension.

CASE V.—Male patient; at first observation had normal blood-pressure and renal function. Six years later, had hypertension with good kidney function.

From this study, however, it may be stated that hypertension in these cases is usually associated with evidences of renal impairment and *vice versa*, except in cases of cardiac failure or vascular collapse. Occasionally a case will be seen with impaired or very poor renal function and normal blood-pressure, and on the other hand hypertension will be noted with normal renal function or with only the slightest evidence of beginning renal impairment.

Incidentally, in the earlier stages of this disease renal impairment is not clinically evident and is found only by studies of the concentrating power of the kidney, the phenolsulphonphthalein test, and blood chemistry figures. As with certain other surgical diseases of the kidney, patients with polycystic kidneys can go about with marked azotemia yet without marked clinical signs and in apparent good health. We have often marvelled at such patients who have been observed with extremely high blood nitrogen figures and hypertension for four to six years before becoming clinically uræmic. This is accounted for only in part by the marked kidney reserve

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we possess. Experimentally, Tuffier,⁵⁴ Bradford,⁵⁵ Allen, Scharf, and Lundin,⁵⁶ Paoli,⁵⁷ Chanutin and Ferris,⁵² and others found that in different animals two-thirds to even one-sixth of the normal kidney tissue present was enough to sustain life. Smith⁵⁸ and Muslow⁵⁹ reported clinical cases of extreme diminution of kidney substance. This ability to live with such little kidney tissue is the one bright feature in congenital cystic disease and suggests the principle of treatment, namely, conservatism.

Blood Count Studies.—Those cases with a normal blood urea and phenolsulphonphthalein excretion had a normal high hæmoglobin and red blood cell count. Two cases with normal urea and phenolsulphonphthalein test showed a secondary anæmia. These cases had lost blood over a long period of time as a result of hæmaturia.

Out of sixteen cases with clinical and laboratory evidences of kidney insufficiency in which full blood count studies were made, two had a normal hæmoglobin and red blood cell count while fourteen showed anæmia with an average hæmoglobin of 63 per cent. The lowest was 30 per cent. The color index of these cases had a tendency to be higher than that of an ordinary secondary anæmia (0.7–1.0), *i.e.* approaching the type of a primary or pernicious anæmia. Brown and Roth⁸¹ noted a relationship between anæmia and renal insufficiency, attributing the former to a disturbed hæmatopoiesis. In cases where there was marked infection in the kidney, the white blood cell count ranged between 16,000 and 28,000, and the polymorphonuclear leucocytes between 75 per cent. and 85 per cent. of the total.

Cystoscopy.—This was performed at least once, and sometimes more often in thirty-four cases. Diagnostically, it was of no help except to reveal the source of bleeding or the location of infection.

X-ray Studies.—Flat plates of the abdomen with the Bucky diaphragm were most helpful in suggesting unilateral or bilateral enlargement of the kidneys and calculi. The most valuable aid to diagnosis was pyelography, especially retrograde pyelography. Fifteen cases were diagnosed by retrograde pyelography and three by excretion pyelography. Of these, two cases had both retrograde and excretion pyelography. Retrograde pyelography was usually more helpful than excretory urography especially in cases with poor kidney function, rendering excretory urography impossible for exact diagnosis. In several cases, the retrograde pyelogram also was not diagnostic; 90 per cent. of the cases, however, showed a typical picture. The characteristic appearance of the pyelogram is well known and may be summarized as presenting a stretched-out, “spidery” appearance with sharp lines instead of the soft curving lines of the normal contour.

Where retrograde pyelography is necessary for diagnosis in cases with marked renal impairment, only non-irritating types of solutions are advised, such as those used for intravenous pyelography. Sodium bromide is contra-indicated. No reactions have been seen when using iopax, skiodan, hippuran, or their derivatives for retrograde purposes.

Associated Lesions of Polycystic Kidney.—Cysts of the Liver.—There is a well-known and definite association of this condition with polycystic kidney disease. In fourteen post-mortem examinations, four cases showed cysts of the liver (28.5 per cent.). A fifth case had an exploratory operation with the evacuation of a large cyst of the liver. There were other small liver cysts present and by palpation, polycystic kidneys were noted. As a rule these hepatic cysts are very small and have no relation to the size of the polycystic kidneys. Lejars³⁹ in sixty-two cases found liver cysts in approximately 28 per cent. of the cases; Ritchie⁴⁰ in eighty-eight cases found a 25 per cent. incidence; while Küster²⁴ in 249 cases found the incidence to be 16.5 per cent. Moschcowitz,¹¹ in a very enlightening study, presented evidence to show that cysts of the liver were congenital anomalies which arose from dilatations of aberrant bile ducts. Cysts of the pancreas, spleen and other organs in association with polycystic kidney have been described but are very rare. Involvement of the pancreas has been observed by Kaufmann,⁴⁵ Braasch,³ Bunting,³⁷ Sears⁶⁰ and others. One of our patients who had diabetes was thought possibly to have cystic involvement of his pancreas. He died at another institution, however, and unfortunately no post-mortem examination was made.

Other congenital anomalies, especially of the newborn, have been mentioned earlier in this paper. Other anomalies of the kidney itself are unusual and do not occur more frequently with polycystic kidney than in general. Washburn⁶¹ reported an autopsy of a case with bilateral double kidneys. There were two distinct pelves and ureters on either side, with bilateral cystic involvement. Barnett⁶² described a case of unilateral fused kidney; the upper kidney was polycystic while the lower, normal-appearing kidney contained a calculus. One of Wobus'³⁸ cases was a seven and one-half months' foetus with a horseshoe kidney fused at the lower poles.

Incidental Conditions Found in Patients with Polycystic Kidneys.—Other diseases present were coronary artery disease, four cases; lues, gall-bladder disease, chronic phthisis, and pneumonia, twice each; and malaria, rheumatic fever, fibroid uterus, post-partum sepsis, diabetes, and lymphosarcoma, once. The presence of coronary sclerosis is easily understood, because of the high incidence of hypertensive vascular disease (24 per cent.). The patient with lymphosarcoma was a forty-four-year-old man with symptoms of malaise and weakness for five months with a tumor mass in the left upper abdomen for one month. The left pyelogram was somewhat suggestive of polycystic kidney while the right was normal. At exploration, besides a polycystic kidney, an adherent retroperitoneal mass was found, crossing the spine. Specimens removed were reported as being lymphosarcoma. Following his discharge from the hospital, the patient did not report to the radiotherapy department and was lost sight of.

Complications.—Calculi.—One of the surprising features of this study was the frequency of associated calculi. As determined by the history,

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X-ray, operation, or necropsy, renal and ureteral calculi were present in fourteen cases (23.7 per cent.). This is a much higher percentage than recorded in other statistics. Sieber²⁶ found eight cases of calculi in 212. In general, the occurrence of calculi in polycystic kidneys is considered uncommon. Many single case reports of this association have been published such as that of Peacock and Corbett⁶³ who describe multiple bilateral calculi in a case of polycystic kidneys with successful operation. In this series, three cases were operated upon for their calculi. A fourth, a case complicated by an obstructing ureteral stone, was treated conservatively.

Rupture.—Rupture of a polycystic kidney has occurred. Traumatic rupture, following the kick of a horse, has been reported by Brin.⁶⁴ One of the cases in this group, non-traumatic in nature, will be described because of its unusual features.

CASE VI.—B. C., male, aged fifty-eight, admitted with left lower quadrant pain of eighteen hours' duration. History of hypertension (220) for many years, also left lumbar colic with passage of stones four years previously.

Physical Examination.—Left costovertebral tenderness and mass in the left iliac fossa. Hæmoglobin, 45 per cent.; white blood cells, 17,000, with 79 per cent. polymorphonuclear leucocytes. Urine: albumin 2 plus, clumped white blood cells, few red blood cells, and granular hyaline casts present. *Diagnosis.*—Retrocolonic abscess.

Operation.—Incision and drainage of large retroperitoneal hæmatoma. *Post-operative course.*—Barium enema showed an extracolonic mass to be pressing on the descending colon. A left pyelogram was typical of polycystic kidney. A right pyelogram showed the same diagnosis. Evidently, the left polycystic kidney had ruptured, resulting in a perirenal retrocolonic hæmatoma. The wound healed after two months. The patient was readmitted seven months later with oliguria and lumbar pain. He died in uræmia with pulmonary œdema.

At post-mortem he had huge bilateral polycystic kidneys, renal and ureteral calculi, left pyelo-ureteral stenosis. Cysts of the liver, hypertrophy of the left ventricle, pulmonary œdema, and bronchopneumonia.

Another case at post-mortem showed one of the cysts completely detached from the kidney, lying free about two inches from the lower pole in the perirenal tissue.

Infection.—This is probably the most important complication of polycystic kidney. Because infection threatens to increase the damage to an already impaired kidney, surgical procedures may be indicated. There are three main types of infection seen. In one type there is found pyelitis, pyelonephritis, or infected hydronephrosis, any of which may be secondary to moderate obstruction at the pyelo-ureteral junction by the pressure of cysts. There may be associated calculi. A second type is purulent infection localized to individual cysts. This is sometimes seen as a complication of blood-stream infection from some other focus, *e.g.*, general sepsis, and was found at post-mortem in one case of this group. A third type is a diffuse purulent infection of the residual renal parenchyma as well as the cysts with occasional complicating perforation and perinephric abscess. (Fig. 2.) Fifty per cent. of the cases showed some degree of mild infection as determined by the urinary findings while 32 per cent. showed definite pus in the urine. Out of 212 post-mortem cases, Sieber²⁶ found twenty-one with

purulent conditions of the kidney. Of the cases in this study, four patients were operated solely because of infection, two of which were for perinephric abscess.

Malignancy of the Kidney Complicating Polycystic Kidney Disease.—No

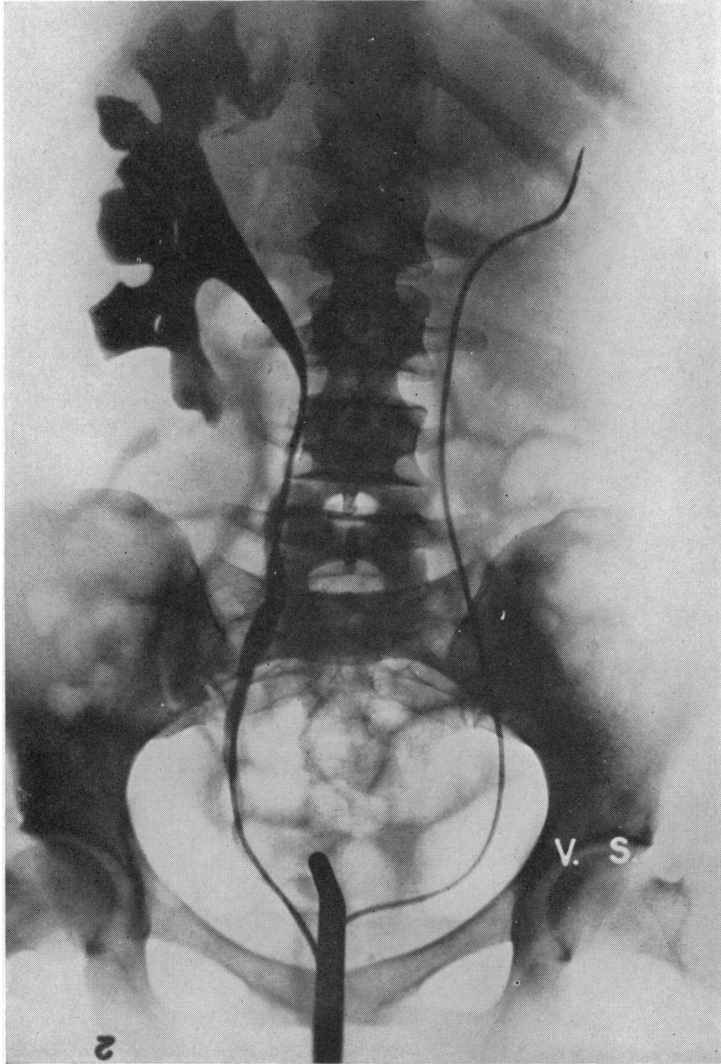


FIG. 2.—Pyelogram of case of bilateral polycystic kidneys. The right kidney was infected. There was an abscess at upper pole with perforation and perinephric abscess.

such cases were seen either clinically or pathologically in this hospital nor were any reports encountered in the literature.*

Renal Tuberculosis Complicating Polycystic Kidney Disease.—This was

* Since this article was accepted for publication, Walters and Braasch (*Surg., Gynec. and Obst.*, vol. 58, No. 3, p. 649, March, 1934) mention three cases of polycystic kidney complicated by malignant disease which were nephrectomized.

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not encountered in this series. Uteau,⁶⁵ Vintici,⁶⁶ and Chauvin and Tristant⁶⁷ have recently reported such cases.

Diagnosis and Differential Diagnosis.—In typical instances the diagnosis of congenital polycystic kidney is relatively simple. A history of loin or abdominal pain, hæmaturia, nocturia, and loss in weight in a patient who has unilateral or bilateral loin masses together with hypertension, and laboratory evidences of renal impairment, is most probable evidence of this disease. A familial history is confirmatory and a pyelogram will invariably prove the diagnosis. On the other hand, sometimes the diagnosis may be obscure and not made during life. This is especially true for cases who are admitted acutely ill or in extremis, or in traumatic cases. Four cases were first discovered on the post-mortem table. They are as follows:

CASE VII.—Forty-three-year-old man; had a carbuncle of the neck; crucial incision. Developed streptococcus hemolyticus sepsis and died.

Post-mortem.—Septicopyæmia, acute bacterial endocarditis, small bilateral polycystic kidneys with suppuration.

CASE VIII.—Fifty-seven-year-old man. Admitted with signs of left lobar pneumonia and cardiac insufficiency. History of hypertension and asthma for two years. Only the enlarged liver was palpable.

Post-mortem.—Moderately enlarged, bilateral polycystic kidneys with a staghorn calculus on one side; liver enlarged and nutmeg; pneumonia, left lung.

CASE IX.—Forty-eight-year-old woman; thought to be a hypertensive cardio-nephritic; died in uræmia; no abdominal masses except palpable liver. Abdominal X-ray was unsatisfactory.

Post-mortem.—Bilateral polycystic kidneys, cardiac hypertrophy, and coronary sclerosis.

CASE X.—Sixty-five-year-old male; had signs of pneumonia and died on the day of admission in coma and collapse.

Post-mortem.—Bronchopneumonia both lower lobes; generalized arteriosclerosis and bilateral polycystic kidneys.

Case IX represents a difficult type to diagnose. When a patient with signs and symptoms of hypertensive cardio-nephritic disease has a unilateral or bilateral lumbar mass, polycystic disease should be suspected. A retrograde pyelogram with a non-irritating solution will clear up the diagnosis.

Renal neoplasm is often justly suspected in these cases. A unilateral renal mass with subjective pain, hæmaturia, and loss in weight is common to both conditions. When a pyelogram of the affected side gives equivocal results, a pyelogram of the opposite kidney will usually settle the diagnosis. However, if this does not show indisputable evidences of polycystic kidney, an exploration must be performed. This was done in four cases.

Unilateral or bilateral hydronephroses or pyonephroses may simulate polycystic kidneys especially with the presence of palpable kidneys, lumbar pain, and evidences of renal insufficiency. Pyelographic studies should make the differential diagnosis. An infected polycystic kidney with a perinephric abscess may so closely resemble a pyonephrosis with perforation that operation may be the only means of recognition of the condition. However, a pyelogram of the opposite side will usually indicate the true condition.

A large spleen, or liver, or echinococcus cyst of the kidney may give

rise to the suspicion of polycystic disease but again pyelography will aid in the diagnosis.

Calculi because of their frequency in this disease may be misleading. This is especially true when dendritic calculi are present or when a ureteral stone blocks the ureter on the side of a unilaterally enlarged kidney. In this situation, as happened in this series, pyelographic study of the affected kidney was not possible or satisfactory and the diagnosis was not suspected.

Causes of Death, Post-mortem Studies and Pathogenesis.—Thirteen cases died without post-mortem examination. Clinically, nine of these died in uræmia. This was complicated in one case by cardiac failure, in another by pneumonia, and in a third by severe anæmia due to hæmaturia. Of thirteen adult cases that were necropsied, nine died in uræmia, two died because of pneumonia, one from a septicopyæmia, and one from intestinal obstruction. Six of the cases showed pneumonia at post-mortem, seven had ventricular hypertrophy, and four showed coronary sclerosis. Chronic passive congestion of the visceral organs was present three times.

A detailed gross and microscopical description of polycystic kidneys is not necessary at this time since several excellent descriptions are available and review of this material has added nothing new. For the same reason, the pathogenesis, with its numerous theories, will be summarized very briefly.

Of the older theories, it might be mentioned that Virchow thought that obstruction of the tubules due either to uric acid and lime deposits or inflammatory changes at the papillæ led to cystic development. Brigidi and Severi⁶⁸ believed that the condition was neoplastic based on the presence of epithelial nests and papillary proliferations in the cysts. Shattock⁶⁹ believed that the cysts developed from cells of Wolffian body remnants. However, the congenital nature of the condition is now well established.

The most generally accepted theory of imperfect development is that founded on the dualistic theory of renal genesis. (Kupfer.⁷⁰) This explains cystic formation as the result of non-union of collecting and of secretory elements which arise from two separate anlagen. This theory was suggested by Koster⁷¹ and developed further by Hildebrand,⁷² and Ribbert.⁷³ Recently, Beeson⁷⁴ has attempted to explain this failure of union as the result of a relative poverty of secretory nephrogenic tissue with an atypical growth of the more abundant tubular collecting and vascular elements.

Kampmeier⁹ believes that cysts develop from a persistence of normally occurring physiological cystic tubules which arise in foetal life. Davis⁷⁵ assumes that polycystic kidney results from a delay in development and differentiation with subsequent cystic changes caused by an inherited defective protoplasm.

Operative Results.—Twenty-three cases (39 per cent.) were operated upon either in this hospital or at other institutions prior to or subsequent to our observation. Two cases had two operations each. The majority of these cases had multiple punctures of cysts and decapsulation with or without

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other procedures. There were four post-operative deaths out of twenty-five operations, or a mortality of 16 per cent. Eight cases had no follow-up record; three cases died within one year after operation, while eight cases lived from one to fourteen years post-operatively.

One case was nephrectomized for polycystic kidney and was alive fourteen years afterwards. One case in which a retroperitoneal hæmatoma was evacuated, and one case explored in which a retroperitoneal sarcoma was found are described earlier in this paper.

Four patients had simple exploratory laparotomy for abdominal masses; nothing was done to the polycystic kidneys which were found. There was no mortality or follow-up.

Four patients had lumbar explorations for suspected renal neoplasm. Decapsulation and puncture of multiple cysts were performed. One patient died following operation; two were not followed and one was alive after eight years.

Three patients were operated upon primarily for complicating calculi. Multiple puncture of cysts was done. There was no mortality. One died from intestinal obstruction three months after leaving the hospital, and in two the follow-up data were incomplete.

Four patients were operated upon because of complicating infection. One of the earlier cases had a nephrectomy for pyelonephritis with multiple abscesses and died. Another case with an infected hydronephrosis, cortical abscesses, and perinephric abscess died following incision and drainage with nephrotomy. A third case had nephrotomy and drainage for pyonephrosis, multiple abscesses, and perinephric abscess on one side followed by a drainage operation on the other side two years later. This patient is well four years after the original operation. Another case is well one year following a nephrotomy and decapsulation.

Of five other operative cases, one was operated upon because of the insistence of the patient's family. This patient had been operated upon two years before with some beneficial result. He was uræmic, and the second kidney was subjected to multiple punctures following which he died. Two cases with punctures of many cysts were alive six months and two years post-operatively. Of two cases that had a nephrotomy and drainage, one died after two months and the other after thirteen years. The cause of death in both cases was uræmia.

Judged by the literature, it would seem that operative procedures in this condition have a high mortality. Brin⁷⁶ reported 117 nephrectomies with a 29 per cent. mortality and twenty-two nephrotomies with a 31.8 per cent. mortality. Mikaniewski⁷⁷ calculated 30 per cent. deaths in 127 nephrectomies and 45 per cent mortality in twenty-seven nephrotomies.

From our observations, it would seem that when very marked renal impairment with uræmia occurs, decapsulation and evacuation of cysts by puncture do not help. On the other hand, when renal impairment with nitrogenous retention occurs, mainly the result of superimposed infection,

a drainage operation may be of value if the infection subsides, provided there is enough functioning renal tissue present to carry on life.

Treatment.—As indicated earlier, the treatment of polycystic kidney disease must be conservative. The same medical treatment should be advised that is given to any chronic nephropathy irrespective of the cause. This includes rest, avoidance of physical or mental stress or exposure to infection, and dietetic regulations which have for their aim the prevention of any overloading of function or irritation of a diseased kidney.

Where pyelitis or pyelonephritis complicates the condition, catheter drainage and pelvic lavage with weak silver solutions may be tried with advantage.

In general, renal operations of any kind are emphatically contra-indicated. This applies to decapsulation, Rovsing's⁷⁸ puncture and evacuation of cysts, Payr's⁷⁹ ignipuncture of cysts, nephrotomy and nephrectomy. It must be remembered that these patients are often living on a minimum of renal tissue and anything, such as an operation, which may disturb the delicate balance is extremely risky.

There are times, however, when surgical procedures are indicated and are even life-saving. Exploratory operations for suspected renal neoplasm will be performed in a number of cases in spite of the most careful diagnostic procedures. In this situation, Rovsing's multiple punctures should be carried out because of the marked diminution in the size of the kidney which results. Theoretically, this diminishes the intrarenal pressure, although the benefit which actually results is questionable, and also diminishes the pressure against extrarenal organs. The latter point was well demonstrated in two instances. In one case, gall-bladder colic was probably caused by a cyst in the right kidney pressing against the junction of the cystic and common ducts and was relieved by puncture of the cysts. A second case with symptoms of marked duodenal pressure was relieved following puncture.

When diffuse suppuration, perhaps with perinephric abscess, occurs with persistently high temperature, elevation of blood-nitrogen figures, and a progressive down-hill course, operation must be performed. A simple drainage, often with nephrotomy, is indicated. A badly infected hydronephrosis with the same accompanying signs and symptoms may also require operation.

Calculous complications may require surgical intervention as when a stone blocks the ureter or a pelvic stone obstructs the pyelo-ureteral junction and conservative cystoscopic measures have failed. Surgery should not be employed in other stone cases.

Nephrectomy should never be done except possibly in cases of persistent suppuration in which other surgical procedures have failed and death may result from continued infection.

An occasional case may occur where the pressure of the enlarged kidney will give symptoms that make life unbearable. These cases can be relieved by multiple punctures and evacuation of cysts. Undoubtedly the change in intrarenal pressure resulting from such an evacuation may be detrimental by disturbing the internal renal balance of pressure relationships. These

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studies have shown that patients without complication live longer without operation than those who have been operated upon.

Only occasionally will persistent loss of blood in the urine endanger the patient's life. Most cases will respond to rest, or transfusion, and, sometimes, pelvic lavage with astringent solutions. Hypertensive subjects will probably be benefited at times by the loss of blood. In the rare cases of severe bleeding, operation with multiple punctures may be advised.

The prevention of this disease would appear to be dependent upon the avoidance of progeny in cases with a familial history. Certainly, in a family, as reported by Fuller⁸⁰ where cases occurred in four generations and affected nine out of twenty-seven individuals, the bearing of children should be discouraged.

Summary.—An anatomical definition of polycystic kidney is given. While for practical purposes the disease may always be considered bilateral, two proved unilateral cases are described. Evidence is presented to show that the disease as seen in the newborn and in adults is the same condition. The study is based on one infant case and fifty-nine adults. The average age at the onset of symptoms is 41.5 years while the average age at death is fifty years. Forty-three per cent. of the cases are dead. The familial and hereditary nature of this congenital condition is emphasized. The symptoms presented serve to divide the cases into eight main clinical groups. The most common symptoms are loin and abdominal pain, hæmaturia (56 per cent.), nocturia, loss in weight, vomiting and tumor mass. Both kidneys were palpated in 66 per cent. of the cases. The liver was enlarged in 25.4 per cent. of the cases while liver cysts were present in 28.5 per cent. of the post-mortem examinations. The heart was enlarged in 30.5 per cent. and arteriosclerosis was present in 23.7 per cent. of the cases. The frequency of ocular fundus changes is noted. Laboratory evidence showed 71 per cent. of the cases to have renal impairment at one time or another. Fifty-seven per cent. of the cases had hypertension. Its relation to renal impairment is discussed. An associated anæmia with a relatively high color index is found. An unusually high percentage of calculi (23.7 per cent.) complicated these cases. Urinary findings indicate that severe infection was present in 32 per cent. of the cases. The use of non-irritating solutions for retrograde pyelography is advised. The diagnosis and differential diagnosis are discussed. The treatment is conservative, medical. Operation should never be done except for complications, as diffuse suppuration, certain calculous conditions, and for other rare indications which are detailed.

Thanks are due to the attending physicians and surgeons of the Mt. Sinai Hospital for permission to use the cases which were admitted to their respective services. I am also indebted to Dr. Max Lederer for the use of the pathological material of the Jewish Hospital of Brooklyn.

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