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Invited review

Renal cysts in pediatric patients

A classification and overview

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Abstract. Renal cysts are relatively common. They may be single, multiple, or innumerable, cortical or medullary. Most renal cysts are spherical, thin-walled, epithelial-lined structures that contain fluid with features of a plasma ultrafiltrate. A clinically useful classification must include characteristics such as age of onset, family history and association with extrarenal lesions, as well as morphologic parameters. Renal dysplasia is disturbed renal histogenesis, either syndromic or non-syndromic, which usually gives rise to morphologically characteristic renal cysts. Two important and distinctive familial forms of renal polycystic disease occur. Autosomal dominant polycystic disease characteristically becomes manifest in adulthood but is becoming increasingly diagnosed in young individuals. Autosomal recessive infantile polycystic disease has complex relationships with "congenital hepatic fibrosis". Other cystic renal lesions are less common in young patients, but their occurrence in association with other abnormalities provokes speculation regarding pathogenesis.

Key words: Renal cysts – Renal dysplasia– Polycystic renal disease – Autosomal dominant (adult) polycystic renal disease – Autosomal recessive (infantile) polycystic renal disease – Congenital hepatic fibrosis – Renal medullary cystic disease – Acquired renal cystic disease

Introduction

Renal cysts are relatively common lesions. They may be solitary, multiple or innumerable, cortical or medullary, familial or sporadic, associated with extrarenal lesions or not, and may become recognized at any age.

Morphologically, renal cysts are usually relatively simple lesions: spherical, thin-walled, lined by non-specific simple epithelium and containing fluid with chemical features of an ultrafiltrate of plasma. Consideration of many other attributes, epidemiologic, demographic, genetic, clinical, and phenomenologic as well as conventional or more sophisticated morphology, currently makes possible a system of classification that has predictive features. The proposed system of classification (Table 1) has evolved over decades, [1, 2] and is in essential agreement with classifications proposed by friends and colleagues interested in the problem [3, 4]. In the interest of brevity, the classification does not include extra-parenchymal or non-parenchymal cystic lesions in the region of the kidney: hemangiomas, lymphangiomas, calyceal diverticula, teratodermoid cysts and endome-

Table 1. Classification of renal cysts

I.	Renal cystic dysplasia:
	A. Multicystic kidney (total renal dysplasia)
	B. Cystic dysplasia with urinary tract obstruction
	C. Segmental dysplasia (with ectopic ureterocele)
	D. Diffuse cystic dysplasia (with teratogenic syndrome and non-syndromal)
II.	Polycystic renal disease:
	Autosomal recessive polycystic disease (ARPD)
	Autosomal dominant polycystic disease (ADPD)
III.	Glomerulocystic renal disease
IV.	Medullary renal cysts:
	A. Medullary sponge kidney
	B. Medullary cystic disease
V.	Simple renal cysts and multilocular cystic nephroma
VI.	Acquired renal cycstic disease

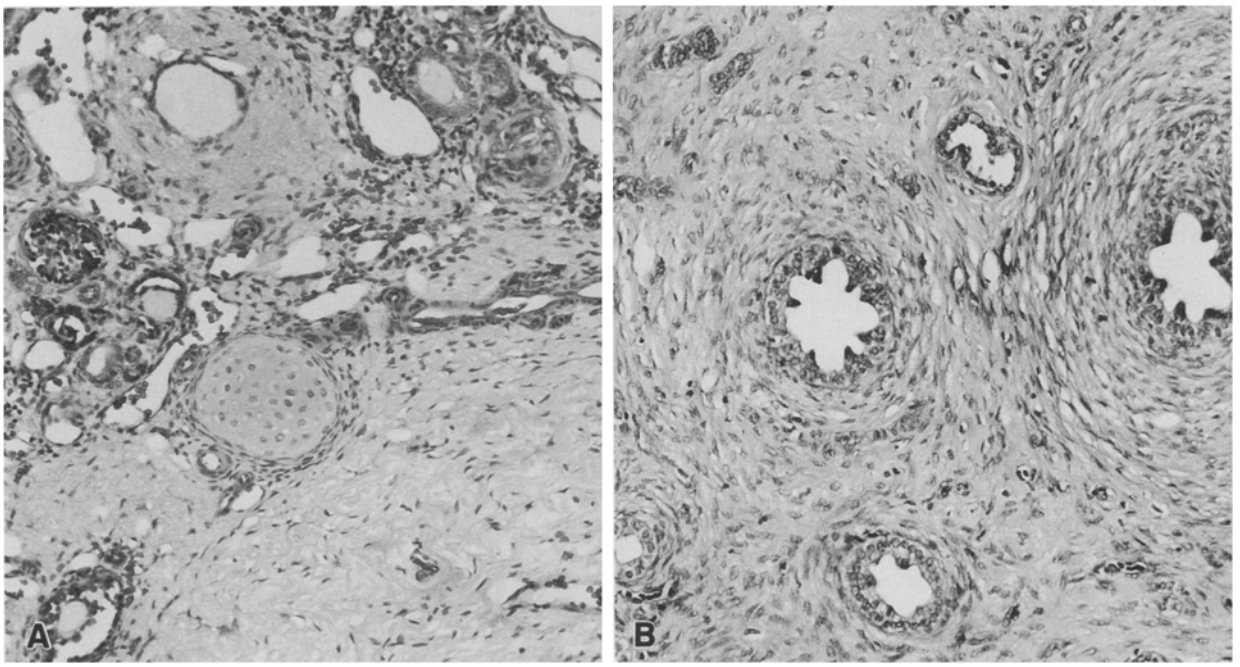

Fig. 1 A, B. Photomicrographs of renal dysplasia. A dilated structure lined by columnar epithelium is surrounded by a cuff of undifferentiated spindle cells (**A**). A spicule of hyaline cartilage is present in the renal interstitium (**B**)

triosis. Importantly, systematic terminology should be relatively unambiguous, relatively independent of methodology, and relatively adaptable to modification as new knowledge is acquired.

Renal dysplasia

The commonest renal cystic disorder in pediatric patients is renal dysplasia, a disturbance in renal ontogeny that results in the presence of structures not present during normal nephrogenesis. These structures include: (1) lobular congeries of coiled epithelial structures lined by low cuboidal hyperchromatic cells surrounded by (2) cuffs or mantles of immature spindle cells, (3) dilated epithelial structures lined by tall cuboidal or columnar, occasional secretory cells, and (4) dysontogenic tissue in the interstitium including fat, hematopoietic tissue, disorderly blood vessels, and most typically spicules of hyaline cartilage which can be found in approximately a third of dysplastic kidneys (Fig. 1).

Microdissection of dysplastic kidneys shows that any component of the nephron may undergo cystic distilation, even glomeruli. Potter [5] attributes renal dysplasia (her type 2 cystic disease) to disordered ampullary function. Variations in gross and microscopic configuration presumably result from differences in the time during nephrogenesis when ampullary function becomes deranged.

Defined by microscopic features, renal dysplasia occurs in several phenomenologically defined forms (Table 1). In the commonest of these, multicystic renal dysplasia (which we have termed "total renal dysplasia"), one (rarely both) kidney, or perhaps better "renal masses" since they do not look like or function like kidneys, presents as a disorderly aggregate of variable-sized epithelial-lined structures loosely aggregated by flimsy grey-white connective tissue (Fig. 2). The multicystic dysplastic kidney is not only the commonest cystic renal lesion in pediatric patients, but is the commonest abdominal mass in newborn infants. The urether which subserves the dysplastic mass is practically always abnormal, either absent, discontinuous or atretic. The dogma is that normally differentiated nephrons are not present in a multicystic ("totally") dysplastic kidney as one would expect if the ureteric bud was congenitally absent. This, of course varies depending upon when the ureteric bud becomes abnormal. Occasional normally differentiated nephrons may be found in multicystic kidneys.

The contralateral kidney is usually normal except for compensatory hypertrophy. Kidneys contralateral to multicystic dysplastic kidneys are slightly more disposed to positional or rotational anomalies or to minor degrees of ureteropelvic stenosis than are kidneys whose opposite number is normal [6, 7]. In spite of this fact, if a kidney

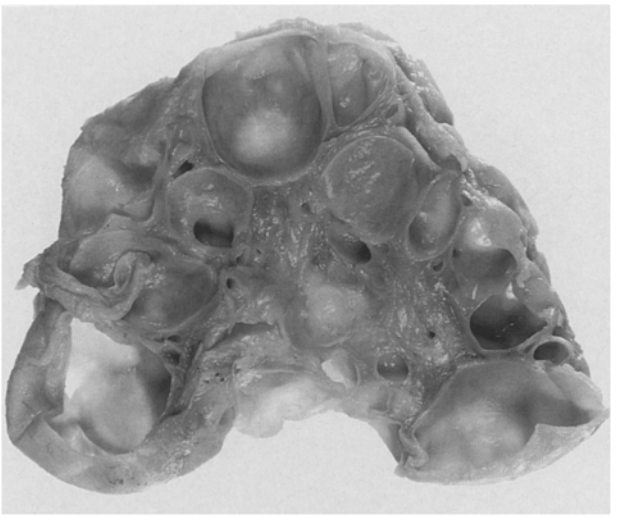

Fig. 2. Gross photograph of a multicystic dysplastic kidney. The renal mass consists of variably sized cysts with no grossly recognizable renal parenchyma

contralateral to a multicystic dysplastic kidney is found by relatively simple studies (intravenous urography or ultrasound) to be normal, its prognosis for continuing function is excellent. Particularly, it can be stated with great confidence that it will not become cystic. There are very rare reports of multicystic dysplastic kidneys serving as a source of sepsis, associated with hypertension, or coming to harbor tumors [8].

Disorders of other organ systems are importantly but not invariably associated with multicystic renal dysplasia. They include esophogeal or other gastrointestinal atresia, impaired cardiac septation, either atrial or ventricular, and disturbed neural tubularization such as lumber meningomyelocele. These associations are manifestations of the biogenic law that states that the association of malformations correlates with the time during ontogeny at which an insult occurs rather than with the nature of that hypothetical insult.

We have seen multicystic dysplastic kidneys in siblings and in twins (and also in one of identical twins), but this appears to be coincidental occurrence of a relatively common malformation. For purposes of genetic counselling, typical examples of multicystic renal dysplasia can be regarded as sporadic. Some reservations attend the very uncommon bilateral examples which may conceivably represent variable expressions of pleomorphic hereditary syndromes or "private" syndromes.

Microscopic features of renal dysplasia are common in congenitally obstructed kidneys. The obstructing lesion is usually bilateral, with urethral valves or urethral atresia, or associated with the "prune belly syndrome." Potter [5] designates this association as her type 4 cystic disease, but her nephron dissections and diagrammatic representation of the abnormality do not differe qualitatively from her type 2 cystic disease. We regard what we call "obstructive dysplasia" as constituting bilateral, if asymmetric, examples of renal dysplasia of which the cause, obstruction during nephrogenesis, is known.

Table 2. Types of renal dysplasia

I.	Multicystic (total) renal dysplasia
II.	Obstructive renal dysplasia:
	A. Associated with lower tract obstruction
	B. Segmental renal dysplasia (with ectopic ureterocele)
III.	Diffuse renal dysplasia, syndromal and non-syndromal

A more narrowly specific and provocative example of "obstructive dysplasia" is the very frequent presence of dysplastic microscopic features in the (almost invariably cephalic) atrophic pole of a kidney served by a duplicated collecting system that terminates in an ectopic ureterocele [2]. This sporadic lesion has characteristic epidemiology (predominance in girls) and clinical manifestations (wetness between episodes of normal voiding). It should be emphasized that the presence of dysplastic features in the atrophic segment of kidney drained via an ectopic ureterocele does not contribute to the clinical features of the syndrome, rather they are an interesting association of renal dysplasia occurring following obstruction during nephrogenesis.

Microscopic features of dysplasia constitute the renal lesion of many multisystem syndromes (Table 2), most commonly autosomal recessive in their inheritance, [2, 9] less commonly associated with aneuploidies, especially trisomy 13 [10, 11]. These associations therefore differ from the more common sporadic expressions of renal dysplasia in that they are genetically, or if not classically mendelian, at least chromosomally mediated. It should be emphasized that with some exceptions such as the Meckel-Gruber syndrome and its variants, renal participation in these syndromes is not clinically or functionally predominant but constitutes important "trademarks" of the syndromes. Often the predominant morphologic expression of the renal involvement is the presence of rows of ectatic glomeruli beneath the renal capsule.

The ectatic glomeruli associated with teratologic syndromes are encompassed in cuffs of variably differentiated spindle cells. Lobules of dys-

plastic tissue are usually present in deeper portions of the kidneys. Table 2 cites only a few syndromes with which renal cysts may be associated [12–15].

Renal lesions are important components of a few autosomal dominant hereditary syndromes, notably tuberous sclerosis and the von Hippel-Lindau syndrome, less significantly von Recklinghausen's neurofibromatosis. These renal lesions are not necessarily "dysplastic" as defined above.

The most readily recognized renal lesion in tuberous sclerosis is the angiomyolipoma, a hamartomatous aggregate of fat-filled cells, vascular smooth muscle cells and epithelial-lined structures. Angiomyolypomas may be found as inconsequential lesions at autopsy and, if multiple, this should raise the possibility of tuberous sclerosis. More specific is the presence of ectatic or cystically dilated tubular segments lined by tall, hypergranulated cells [16, 17]. Tubular proliferative lesions occur, varying from tubular adenomas to frank renal cell adenocarcinomas. Renal cysts may diffusely involve the kidney in tuberous sclerosis and may invite confusion with precociously expressed autosomal dominant (adult) polycystic renal disease [18, 19].

Tubular ectasias and proliferative lesions occur in the von Hippel-Lindau syndrome. These vary from tubular cysts to renal cell adenocarcinoma [20]. The renal lesion of von Recklinghausen's neurofibromatosis is the occasional occurrence of periarterial neurofibromatosis, which may give rise to renovascular hypertension.

Polycystic renal diseases

Polycystic renal disease has come to be defined as an hereditofamilial disorder in which functionally significant portions of renal parenchyma become converted into epithelial-lined ectatic spaces. Two forms are currently recognized (Table 3). They differ in mode of inheritance, morphology and associated abnormalities. Paradoxically, the distinction between the two forms has been recently blurred in regard to perhaps the most basic difference, namely the age at clinical recognition.

Autosomal recessive polycystic disease

Autosomal recessive polycystic disease (ARPD) was formerly called infantile polycystic disease. The current designation embodies the recognition of its genetic mechanism and also the variable age at which the disease becomes clinically recognized.

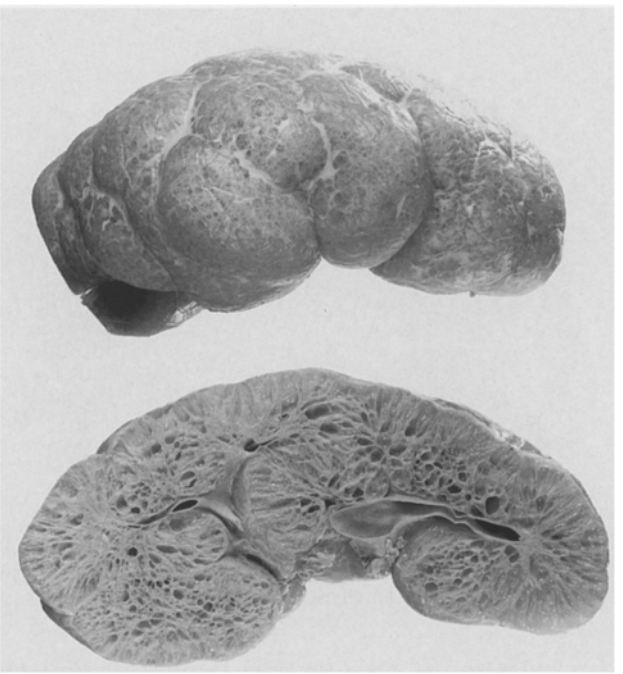

Fig. 3. Gross photograph of autosomal recessive polycystic kidneys from a newborn infant. The surface is smooth and studded with minute opalescent dots. The cut surface is radially traversed by fusiform ectatic spores

The kidneys in ARPD are greatly enlarged but are smooth and reniform. The collecting systems are normal. The capsular surfaces of the kidneys are uniformly studded by minute opalescent dots which, on the cut surface, can be recognized as the capsular extent of innumerable cylindrical or fusiform ectatic spaces (Fig. 3). Microscopically these spaces can be recognized as dilated collecting ducts. Between these are wedges of normally differentiated nephrons (Fig. 4). Microdissection

Table 3. Renal cysts associated with teratogenic syndromes

I.	Cystic dysplasia associated with autosomal recessive syndromes:
	A. Meckel-Gruber syndrome and variants (Miranda-Feingold, Dandy-Walker, etc.)
	B. Orofacial digital syndrome
	C. Zellweger cerebro-hepato-renal syndrome
	D. Short limb polydactyly syndromes
	E. Jeune asphyxiating thoracic dystrophy
	F. Miscellaneous
II.	Cystic (and other renal lesions) associated with autosomal dominant disorders:
	A. Tuberous sclerosis
	B. von Hippel-Lindau syndrome
	C. von Recklinghausen's neurofibromatosis
III.	Cystic lesions associated with aneuploidies:
	A. Trisomy 13 and trisomy 18
	B. Turner syndrome

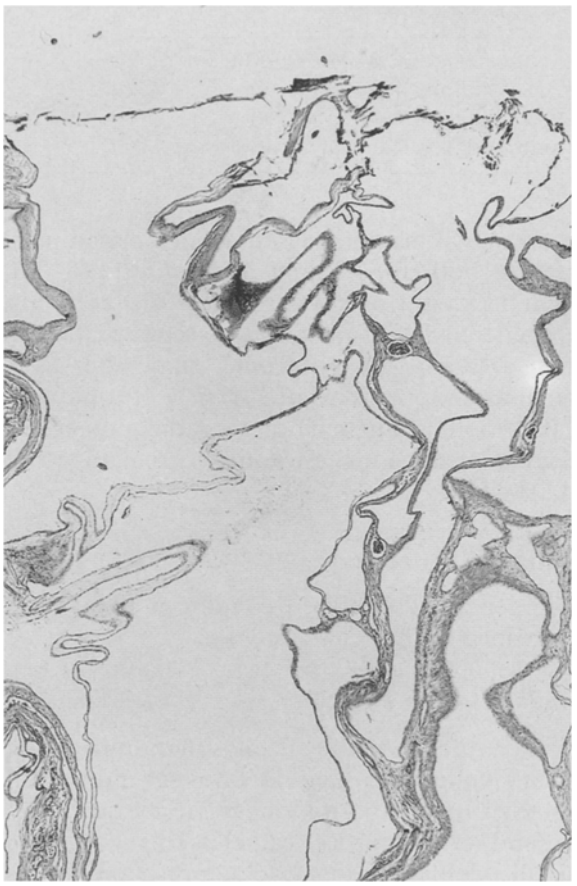

Fig. 4. Photomicrograph of an autosomal recessive polycystic kidney. The ectatic spaces are collecting ducts

[5] and scanning electron microscopy confirm the identification of the ectatic spaces and show that obstruction of urinary flow is not a component of ARPD.

Every case of ARPD has an abnormality of the liver that consists of compressed disc-shaped dilation of periportal biliary ductules [9, 21]. Widespread intrahepatic and extrahepatic dilation of bile ducts is referred to as Caroli disease [22]. Congenital anomalies of other organ systems are distinctly uncommon [22].

About half of the individuals with ARPD are stillborn or die in the perinatal period, usually of pulmonary insufficiency. Prolonged survival is accompanied by severe hypertension and congestive heart failure. Occasional survival into the thirties occurs. In long survivors, hepatic involvement leads to portal venous hypertension and its complications, bleeding from esopogheal varices and intractable ascites. The suggestion that the variable age expression of ARPD is genetically mediated [23] is certainly an over-simplification [24]. The heterogeneous syndrome of congenital hepatic fibrosis (CHD) includes not only rare examples of long survivors of ARPD, but cases with a few spherical epithelial-lined renal cysts, not resembling the renal lesion of ARPD and clinically silent, and many cases in which the kidneys are normal [25].

Autosomal dominant polycystic disease

Autosomal dominant polycystic disease (ADPD) is more common than ARPD and is a cause of progressive renal failure well recognized by internists, nephrologists and pathologists. An incidence of perhaps one case among a thousand hospitalized patients is a useful approximation. Until recently most cases of ADPD remained unrecognized until about the age of 40 years when bilateral flank masses, hypertension or radiographic studies led to the diagnosis. Survival thereafter was measured by years and, unless prolonged by dialysis or transplantation, the average age at death was about 50 years. The occurrence of progressive renal disease in siblings, parents, grandparents, aunts, and uncles is typical [26].

About a third of cases with ADPD have one or a few epithelial-lined cysts of the liver. Unless life is prolonged by dialysis or transplantation, these are almost always clinically unimportant. Cysts occur less commonly in other organs. More important is the association of ADPD and cerebral arterial aneurysm. About 15% of cases of ADPD die of subarachnoid hemorrhage from a ruptured arterial aneurysm. About 3% of cases of ruptured arterial cerebral aneurysms are in patients with ADPD, sometimes as an initial manifestation.

The kidneys in ADPD are enormous, each often weighing 2000 g or more in an adult. The parenchyma is studded throughout cortex and medulla with spherical cysts relatively uniform in size, a few centimeters in diameter (Fig. 5). Unless altered by hemorrhage, the content of the cysts is a thin clear straw-colored fluid.

Microscopically, cysts in ADPD are usually lined by simple cuboidal epithelium occasionally characteristic of specific segments of the nephron [5]. Microdissection verifies that the cysts arise from any segment of the nephron. In fact, the cysts in ADPD are not sequestra but are localized eccentric diverticula that retain communication with nephrons. Micropuncture studies have shown that the cysts resorb glucose and secrete urea [27].

Although involvement of the two kidneys may be asynchronous or assymetric, the disorder is intrinsically bilateral. Rare apparently unilateral cases are not understood [28, 29].

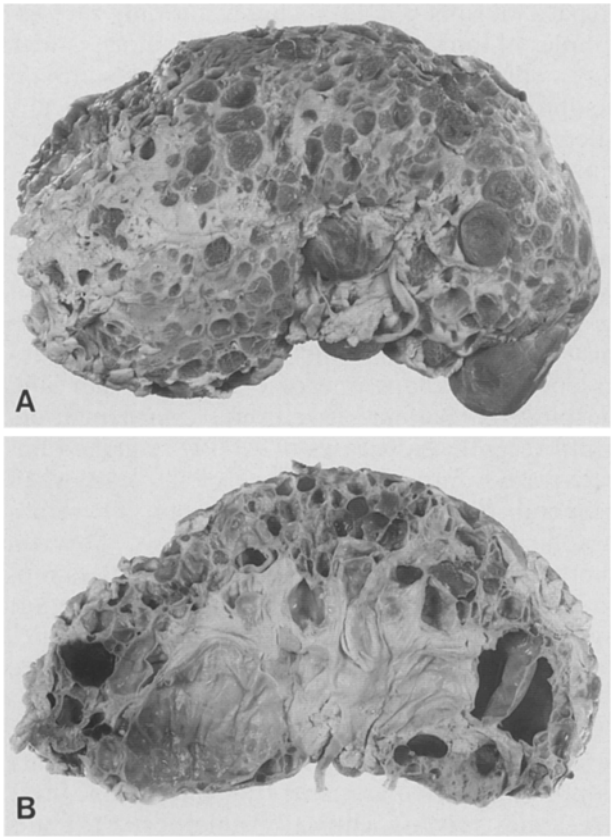

Fig. 5 A, B. Gross photographs of autosomal dominant polycystic kidneys from an adult. The surface is bossellated and the cut surface displays innumerable spherical relatively uniformly sized cysts throughout the cortex and medulla

The question of the early renal morphology in patients destined to manifest ADPD in middle life has been mooted for generations. Recently non-invasive studies of members of families with ADPD or surveillance of family members for potential renal donation has partially answered this question. Renal cysts have been recognized in relatives of patients with ADPD in childhood, infancy, and even in fetuses in utero [30, 31]. The genetic locus has recently been assigned to autosome 16 [32]. There have, however, been cases of phenotypically typical ADPD which have not been attributable to an abnormal gene on the 16th autosome [33].

Glomerulocystic disease

Glomerulocystic disease designates cases of widespread cystic ectasia of renal glomeruli. As described above, cystic dilatation of renal glomeruli is a component of renal dysplasia. Glomeruli participate in the dilatation of elements of the nephron in ADPD. Cystic ectasia of glomeruli occurs

Table 4. Polycystic renal disease

I.	Autosomal recessive polycystic disease (ARPD)
	A. Congenital hepatic fibrosis
	B. Caroli's disease
II.	Autosomal dominant polycystic disease (ADPD)

with other malformations and as an isolated malformation both in children and adults [34, 35]. "Glomerulocystic disease" is therefore certainly heterogeneous [34], sometimes as renal participation in a teratologic syndrome, sometimes as a precocious expression of ADPD (Table 4). Whether there is a genetic or sporadic glomerulocystic disease outside these concepts remains to be established [36, 37].

Medullary renal cysts

In two generically defined conditions renal cysts are confined to the renal medulla.

Medullary sponge kidney

Medullary sponge kidney is the situation in which papillary collecting ducts in one, several, or all papillae of one or both kidneys are cystically dilated and often harbor calculi. This condition originally defined by its pyelographic picture as the "sponge kidney," is overwhelmingly a disorder of adults which produces clinical manifestations as complications of calculous disease and is rarely a pediatric problem [38].

Renal medullary cystic disease

Renal medullary cystic disease is quite another, and very complex problem [39]. Medullary cysts may occur in certain hereditofamilial syndromes such as the Jeune syndrome and Bardet-Biedl syndrome [40]. Pedigrees have been reported in which medullary renal cysts occurred in association with hepatic biliary proliferations, portal fibrosis, and portal hypertension [41]. In long survivors with ARPD, medullary cysts may become prominent and more nearly spherical rather than fusiform.

In addition to these expressions, there is a group of cases with progressive renal insufficiency in the first two decades of life often with urinary salt and water wasting, in which progressive renal contraction occurs and in many of whom small to medium-sized (a few to several millimeters in diameter) epithelial-lined cysts are described at the corticomedullary junction. The cysts characteristically do not obviously communicate with nephrons.

Table 5. Glomerulocystic renal disease

I. Autosomal dominant polycystic disease
II. Associated with renal dysplasia, syndromic or non-syndromic
A. Multicystic renal dysplasia
B. Obstructive renal dysplasia
C. Syndromic renal dysplasias
III. Sporadic glomerulocystic disease

Table 6. Medullary renal cystic diseases

I. The medullary sponge kidney
II. Medullary cystic disease:
A. Familial juvenile nephronophthisis (Fanconi)
B. (Uremic) medullary cystic disease
C. Variants:
1. with pigmentary retinal dysplasia
2. with hepatic fibrosis
3. other syndromes (Jeune, Bardet-Biedl, etc.)

The cortical contraction is morphologically non-specific, consisting of interstitial fibrosis and banal chronic inflammation, periglomerular and peritubular basement membrane thickening and tubular atrophy [42]. Familial aggregation occurs, usually in a recessive pattern, although some pedigrees are compatible with dominant inheritance, and the distribution between the sexes is not uniform. The disorder is not rare.

Although there has been some emphasis on the cysts in this group of cases, cases of progressive renal insufficiency without cysts occur in families with cases that have cysts. Specifically it is not believed that the cysts are a major pathogenic factor in the disorder. Currently it is thought that these disorders represent familial examples of tubulointerstitial nephritis of as yet unestablished pathogenesis [4].

Some authorities adapt a unitarian approach to this group of cases, while others emphasize clinical, demographic and genetic differences that tend to separate a group of cases of Fanconi's familial juvenile nephronophthisis type from uremic medullary cystic disease, per se, plus a variant with variously characterized retinal lesions [43, 44]. The problem of classifying these syndromes remains unresolved. Currently important are the facts that: (1) cysts, even if present, may be of a size not currently detected by radiographic or other imaging techniques; (2) renal biopsy usually fails to demonstrate the cysts, if any, and cortical histologic alterations are non-specific; (3) clinical and renal functional aspects of a case, although collectively suggestive, are intrinsically non-specific, particularly if familial aggregation of cases is not present or not detected (Table 5).

Localized unilateral, and segmental renal cysts

In a heterogeneous group of situations, a renal mass is detected which proves either on in vivo studies or pathologically to be cystic. Grouping these cases together has no implications of a common pathogenesis but merely emphasizes the common denominator of clinical presention, usually as renal masses [45].

Simple renal cysts, lesions familiar as incidental findings at autopsy in adults are either single or multiple, cortical or medullary. Their increasing frequency with advancing age and association with acquired renal diseases supports the suggestion that they are acquired lesions. In view of their frequency, they are rarely a clinical problem. If numerous and bilateral, multiple simple cysts may enter the differential diagnosis of ADPD.

True neoplasms of the kidney, whether Wilms' tumor (nephroblastoma) or renal cell carcinoma, may be grossly cystic either by imaging techniques or pathologic study. There is also an uncommon lesion variably designated "multilocular cystic nephroma" or "multilocular renal cyst" with distinctive (if variable) morphology and a usually benign clinical evolution [2].

Acquired renal cystic disease

Development of cysts or proliferative epithelial lesions in native kidneys of patients with end-stage renal disease has become well recognized since its description by Dunnill et al. [46]. Usually, the patients have been maintained on long-term hemodialysis, less commonly peritoneal dialysis [47]. Although there are unexplained variations, duration of support is the major factor in the pathogenesis of acquired renal cystic disease. Tubular epithelial hyperplasia, cysts, adenomas or lesions recognizable as renal adenocarcinomas occur. Truly malignant clinical evolution occurs [48].

Conclusion

Renal cysts are a very complex phenomenon. Until recently, systematization of renal cystic disorders has drawn heavily on examination and codification of descriptive data, tedious, even pedantic except to devotees. Necessarily, gaps have existed in systems of classification based on such information. Recently, at least some of those gaps have narrowed. Paradoxically, at the same time

that renal cystic disorders can be increasingly recognized outside their ages of clinical expression by such techniques as ultrasonography, a fact that might superficially be presumed to blur distinctions among them, techniques drawn from modern cell biology, such as linkage analysis using DNA probes, have sharpened some of the diagnostic distinctions. The practically exposed among us, whether family practitioners, nephrologists, radiologists or renal morphologists, can continue to assist in these advances by maintaining and, when possible, increasing the accuracy and precision with which we study an example of a renal cystic lesion. Areas to which we can contribute include: personal and family history including age at onset, sex, and associated disorders in the propositus or in the family, and availability of clinical, radiographic, or morphologic studies available in members of the family.

References

1. Gleason DG, McAlister WH, Kissane J (1967) Cystic diseases of the kidney in children. Am J Roentgenol 100: 135–146
2. Kissane JM (1983) Congenital malformations. In: Heptinstall RH (ed) Pathology of the kidney, 3rd eds. Little Brown & Co, Boston, pp 83–140
3. Bernstein J (1976) A classification of renal cysts. In: Gardner KD Jr (ed) Cystic diseases of the kidney. Wiley, New York, pp 7–30
4. Spence HM, Singleton R (1972) Cysts and cystic disorders of the kidney: types, diagnosis, treatment. Urol Surv 22: 131–158
5. Potter EL (ed) (1972) Normal and abnormal development of the kidney. Year Book Medical Publishers, Chicago
6. Avni EF, Thoua Y, Laimand B, Didier F, Droulle P, Schulman CC (1986) Multicystic dysplastic kidney: evolving concepts. In utero diagnosis and post-natal follow-up by ultrasound. Ann Radiol (Paris) 29: 663–668
7. Kleiner B, Filly RA, Mack L, Callen PW (1986) Multicystic dysplastic kidney: observations of contralateral disease in the fetal population. Radiology 161: 27–29
8. Hartman GE (1986) The dilemma of the multicystic dysplastic kidney. Am J Dis Child 140: 925–929
9. Bernstein J (1986) Hepatic and renal involvement in malformation syndromes. Mt Sinai J Med 53: 421–428
10. Bartman I, Barraclough G (1965) Cystic dysplasia of the kidneys studied by microdissection in a case of 13–15 trisomy. J Pathol 89: 233–238
11. Mottet NK, Jensen H (1965) The anomalous embryonic development associated with trisomy 13–15. Am J Clin Pathol 43: 334–347
12. Bernstein J, Brough AJ, McAdams AJ (1974) The renal lesion in syndromes of multiple congenital malformations: cerebrohepatorenal syndrome: Jeune asphysiating thoracic dystrophy: tuberous sclerosis; Meckel syndrome. In: Bergsma D (ed) The Fifth Conference on the Clinical Delineation of Birth Defects, vol X/4. Williams and Wilkins, Baltimore, pp 34–43
13. Poznanski AK, Nosanchuk JS, Baublis J, Holt JF (1970) The cerebro-hepato-renal syndrome (CHRS): (Zellweger's syndrome). Am J Roentgenol 109: 313–322
14. Stapleton FB, Bernstein J, Koh G, Roy S, III Wilroy RS (1982) Cystic kidneys in a patient with oral-facial-digital syndrome type I. Am J Kidney Dis 1: 288–293
15. Tieder M, Levy M, Gubler MC, Gagnadoux MF, Broyer M (1982) Renal abnormalities in the Bardet-Biedl syndrome. Int J Pediatr Nephrol 3: 199–203
16. Bernstein J, Robbins TO, Kissane JM (1986) The renal lesions of tuberous sclerosis. Semin Diagn Pathol 3: 97–105
17. Stillwell TJ, Gomez MR, Kelalis PP (1987) Renal lesions in tuberous sclerosis. J Urol 138: 477–481
18. Mitnick JS, Bosniak MA, Hilton S, Raghavendra BN, Subramanyam B, Genieser NB (1983) Cystic renal disease in tuberous sclerosis. Radiology 147: 85–87
19. Stapleton FB, Johnson D, Kaplan GW, Griswold W (1980) The cystic renal lesion in tuberous sclerosis. J Pediatr 97: 574–579
20. Frimodt-Moller P, Nissen HM, Dyreborg U (1981) Polycystic kidneys as the renal lesion in Lindau's disease. J Urol 125: 868–870
21. Caroli J, Couinaud C, Soupault R, Porcher R, Eteve J (1958) Une affection nouvelle, sans doute congenitale, des voies biliaires. La dilatation kystique unilobaire des canaux hepatiques. Semin Hop Paris 34: 496–502
22. Kaplan BS, Fay J, Shah V, Dillon MJ, Barratt TM (1989) Autosomal recessive polycystic kidney disease. Pediatr Nephrol 3: 43–49
23. Helcyznski L, Wells Tr, Landing BH, Lipsey AI (1984) The renal lesion of congenital hepatic fibrosis: pathologic and morphometric analysis, with comparison to the renal lesion of infantile polycystic disease. Pediatr Pathol 2: 441–445
24. Blyth H, Ockenden BG (1971) Polycystic disease of kidneys and liver presenting in childhood. J Med Genet 8: 257–284
25. Kaplan BS, Kaplan P, Chadarevian J-P de, Jequier S, O'Reagan S, Russo P (1988) Variable expression of autosomal recessive polycystic kidney disease and congenital hepatic fibrosis within a family. Am J Med Genet 29: 639–647
26. Dalgaard OZ (1957) Bilateral polycystic disease of the kidneys: a follow-up study of 284 patients and their families. Acta Med Scand 158 [Suppl 328]: 1–255
27. Bricker NS, Patton JF (1957) Renal function studies in polycystic disease of the kidneys with observations on the effect of surgical decompression. N Engl J Med 256: 212–217
28. Kossow AD, Meek JM (1982) Unilateral adult polycystic kidney disease. J Urol 127: 297–300
29. Lee JKT, McClennan BL, Kissane JM (1978) Unilateral polycystic kidney disease. Am J Roentgenol 130: 1165–1167
30. Kaplan BS, Rabin I, Nogrady MB, Drummond KN (1977) Autosomal dominant polycystic renal disease in children. J Pediatr 90: 782–783
31. Sedman A, Bell P, Manco-Johnson M, Shrier R, Warady BA, Heard EO, Butler-Simon N, Gabow P (1987) Autosomal dominant polycystic kidney disease in childhood: longitudinal study. Kidney Int 31: 1000–1005
32. Reeders STL, Breuning MH, Corney G, Jeremiah SJ, Meera Khan P, Davies KE, Hopkinson DA, Pearson PL, Weatherall DJ (1986) Two genetic markers closely linked to adult polycystic kidney disease on chromosome 16. Br Med J 292: 851–853
33. Romeo G, Devoto M, Costa G, Roncuzzi L, Catizone L, Zucchelli P, Germino GG, Keith T, Weatherall DJ, Reeders ST (1988) A second genetic locus for autosomal dominant polycystic kidney disease. Lancet II: 8–11

34. Joshi VV, Dasznica J (1984) Clinicopathologic spectrum of glomerulocystic kidneys. Report of two cases and a brief review of literature. Pediatr Pathol 2: 171–186
35. Taxy JB, Filmer RB (1976) Glomerulocystic kidney. Report of a case. Arch Pathol Lab Med 100: 186–188
36. Carson RW, Bedi D, Cavallo T, DuBose TD Jr (1987) Familial adult glomerulocystic kidney disease. Am J Kidney Dis 9: 154–165
37. Rizzoni G, Loriat C, Levy M, Milanesi C, Zachello G, Mathieu H (1982) Familial hypoplastic glomerulocystic kidney. A new entity? Clin Nephrol 18: 263–268
38. Kuiper JJ (1976) Medullary sponge kidney. In: Gardner KD Jr (ed) Cystic diseases of the kidney. Wiley, New York, pp 151–171
39. Gardner KD Jr (1976) Juvenile nephronophthisis and renal medullary cystic disease. In: Gardner KD Jr (ed) Cystic diseases of the kidney. Wiley, New York, pp 173–185
40. Donaldson MDC, Warner AA, Trompeter RS, Haycock GB, Chantler C (1985) Familial juvenile nephronophthisis, Jeune's syndrome, and associated disorders. Arch Dis Child 60: 426–443
41. Boichis H, Passwell J, David R (1973) Congenital hepatic fibrosis and nephronophthisis. QJ Med 42: 221–231
42. Waldherr R. Lennert, T, Weber H-P, Fodish HJ, Scharer K (1982) The nephronophthisis complex. A clinicopathologic study in children. Virchows Arch [A] 394: 235–254
43. Bernstein J, Gardner KD Jr (1983) Hereditary tubulo-interstitial nephropathies. In: Cotran RS, Brenner BM, Stein JH (eds) Contemporary issues in nephrology. Churchill Livingstone, Edinburg, London, New York, pp 335–357
44. Senior B (1973) Familial renal-retinal dystrophy. Am J Dis Child 125: 442–447
45. Cho KJ, Thornbury JR, Bernstein J, Heidelberger KP, Walter JF (1979) Localized cystic disease of the kidney: angiographic-pathologic correlation. Am J Roentgenol 132: 891–895
46. Dunnill MS, Millard PR, Oliver D (1977) Acquired cystic disease of the kidneys: a hazard of long-term intermittent maintenance haemodialysis. J Clin Pathol 30: 868–877
47. Hughson MD, Buchwald D, Fox M (1986) Renal neoplasia and acquired cystic kidney disease in patients receiving long-term dialysis. Arch Pathol Lab Med 110: 592–601
48. Bretan PN Jr, Busch MP, Hricak H, Williams RD (1986) Chronic renal failure: a significant risk factor in the development of acquired renal cysts and renal cell carcinoma. Case reports and review of the literature. Cancer 57: 1871–1879