Cysts of various organs have always attracted attention, if only because of their space-occupying character. In recent times their generally innocuous nature and apparently incidental appearance in many conditions have caused them to be relatively ignored. Nevertheless, apart from their morphological dominance in some conditions, they raise many questions of fundamental nature and importance.

An interesting feature of the published material dealing with polycystic kidneys has been the large amount written on causation and mode of formation, with almost complete absence of precise information as to their structure and tissue relations.

This is largely due to the difficulty in obtaining such information, though more gross and imprecise observations are easily made. One of the best methods of gaining detailed data at present available is microdissection. Amongst the infrequent published results in which this technique is used are those of Greene (1922), Lambert (1947), Bialestock (1956, 1958, 1960), Oliver (1960), Baxter (1961a, b), Paatelä (1961), and Osathanondh and Potter (1964).

From these it is apparent that there is a wide range in the distribution of cysts in the nephron and that a study of a large series of cases is necessary to elucidate many of the basic problems. The present paper gives a preliminary statement on some of these cases.

Material and Methods

The specimens were obtained at necropsy from 5 infants, of whom 4 were stillborn and 1 survived for six days after birth, as well as 1 from a child of 4 years. The condition was bilateral in the 6 cases, and, in the first 5, cysts were predominantly corpuscular (glomerular) in origin, while in the sixth renal corpuscles and tubules were equally involved.

The relevant information is given in the Table. Case 6 resulted from the third pregnancy of a mother whose first had been normal. This was followed by twins, one of whom died soon after delivery. Post-mortem examination of this infant showed that the kidneys had appearances similar to the specimen from the case here reported.

Four normal kidneys (that is, those showing neither gross nor histological abnormality), two from babies of 37 weeks' gestation, one at 40 weeks' gestation, and one from

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a child aged 3½ years (attempts to procure renal tissue from a 4-year-old child proved unsuccessful) were obtained for comparison.

The renal tissue was fixed in formol-saline. Appropriate pieces were removed for histological examination. Small tissue wedges were cut and macerated with concentrated hydrochloric acid in accordance with the technique described by Oliver, MacDowell, and Tracy (1951). After maceration was complete, the tissue was washed in water until the immersing fluid gave a constant pH reading when it was concluded that equilibrium had been established. Microdissection technique followed the procedures employed in previous publications (Baxter, 1959, 1960, 1961a, b). The photographs obtained are of unstained microdissected material.

**Results**

**Macroscopical Appearances.** In polycystic renal disease, the kidneys range in gross form from those in which there are minute spaces in the parenchyma (Case 3), to those where the renal substance is replaced by a large mass of scattered or closely-packed thin-walled cysts of various sizes (Case 6).

The external appearance may be normal or there may be large cysts projecting from the surface and thus the over-all organ is much larger than usual. Since corpuscles occur in the cortex, cysts arising from these are more prominent here. A common observation is of numerous small cystic spaces occurring under the capsule. These give a faint granular semi-translucent appearance to the capsule and subcapsular zone (Case 1). At times it has a finely sago-like character.

On sagittal section, cysts of various sizes are scattered through the cortex and the general distribution may not be specially characteristic. However, in typical cases numerous minute cysts give the cortex a somewhat porous impression with a layer of tiny cysts immediately beneath the capsule (Cases 3 and 6). Occasionally the outer rim has a scalloped form due to slightly larger cysts projecting on the surface (Case 5).

In size the cysts may be barely discernible to the naked eye, or pinhead in size, or range from these to examples 2 or more cm. in diameter (Cases 2 and 4). Many cysts of similar size may be grouped together but frequently those of different diameters are intermingled.

The cyst wall is usually thin so that the colour of the contents is apparent. This may be watery, opalescent, or more or less deeply pigmented. Some of the older cysts have thick walls.

Typical cysts of corpuscular origin are confined to the cortical zone and do not extend below the cortico-medullary junction. Nevertheless, there is sometimes involvement of some of the tubules. It is not practicable to distinguish the later stages of the two types of cyst, and occasionally a few are found in the medullary zone. The extreme example is the mixed type (Case 6) in which corpuscles and tubules are approximately equally involved.

**Histological Appearances.** It is important to appreciate that material examined microscopically shows the smallest cysts and therefore attention is directed largely to these; only parts of the walls of larger cysts are viewed and described.

Most of the cysts do not show specially differentiating features. The thin wall has a thin fibrous capsule and is lined by a single layer of cells, usually cuboidal but which may be columnar or flattened. Infrequently, the cells are multi-layered. The contents are homogeneous and lightly staining.

Some cysts have a small glomerular tuft. These range from slightly dilated but otherwise normal corpuscles, through small cysts with well-defined though rudimentary tufts, to those in which the tuft, though still recognizable, has almost completely disappeared (Fig. 1).

Occasionally more than one tuft is present (Fig. 2). In some it seems reasonable to deduce from the pattern that the tuft has become divided into two parts. In others the mechanism of development is not apparent. Very rarely three tuft remnants may be seen.

In the above examples the type of cyst is beyond question. However, many cysts show no such evidence of their nature or origin, and in some of these either their relation to the proximal convoluted tubule or the nature of their vascular supply may still give a clue to their character. Nevertheless, many of the cysts have no feature that would distinguish them out of hand from cysts of the tubules. Their association with indubitable corpuscular cysts may suggest their probable nature and origin. The following features were observed in the renal tissue.

(a) **Capsule.**—This was intact, normal in appearance, and stripped easily in Cases 1, 2, and 3, but was considerably thickened in Cases 4, 5, and 6.

(b) **Cortex.**—The subcapsular cortex was remarkable for the number of renal corpuscles with dilated capsular spaces (Cases 2 and 3), many of which attained cystic proportions (Cases 1 and 4). The cortical parenchymal elements were not reduced to any extent in Cases 1 and 3, but in Cases 2, 4, 5, and 6 there was considerable reduction. In certain areas of these sections the parenchyma was reduced to a few cystic remnants which were encircled by connective tissue. In Cases 5 and 6 the entire sections consisted of a meshwork of connective tissue containing cystic spaces and small blood vessels both of
which were more numerous and larger in Case 6 than in Case 5.

In some of the larger cystic corpuscles hyperplasia, resulting in a heaping up of the lining layer of cells, from 2-3 cells (Cases 1 and 4) up to 5 cells deep (Case 5), was observed.

There was considerable variation in the size and shape of the glomerular tuft of the cystic renal corpuscles. The tuft was sometimes quite large, either filling the capsule (Cases 3 and 4) or surrounded by a well-defined capsular space (Cases 1, 2, and 4). At other times it was small, shrunken, and attached to one side of a large cystic space (Cases 1 and 6). The glomerulus was rounded or digitate in shape (Case 4) and occasionally two tufts were present within the once cystic capsule (Cases 1, 2, and 6). In the largest cysts the glomerular tufts were no longer present.

In addition to the large renal corpuscles in the cortex of Case 3, there was an active subcapsular (nephrogenic) zone in which renal corpuscles and tubules in various stages of maturation appeared.

(c) Medulla.—Changes in the parenchymal elements of the medulla ranged from very slight (Case 3) to gross (Case 5). In Case 4 there was slight reduction in the parenchymal elements accompanied by proliferation of connective tissue elements, and occasional tubules showed dilatation; but in
Fig. 3.—Proximal convoluted tubule from a long-loop nephron showing an enlarged renal corpuscle and over-all tubular dilatation (Case 4). (× 32.) Renal corpuscle, 211 μ diameter; tubule diameter range, 25-112 μ.

Fig. 4.—Low-power enlargement of renal corpuscle and first coils of the proximal tuft (Fig. 3). The renal corpuscle is attached to the tubule by a slender segment. (× 75.)

Fig. 5.—Large cyst with small, insignificant tubular connexion, and a small cyst. Glomerular tufts were not observed in either cyst (Case 6). (× 32.) Large cyst, 2,160 × 1,850 μ; small cyst, 250 × 160 μ.

Fig. 6.—Corpuscular cyst (372 × 310 μ) with obvious glomerular tuft (Case 2). (× 105.)

Fig. 7.—Corpuscular cyst (645 × 385 μ) dissected from subcapsular cortex with small tuft situated at the upper pole (Case 1). (× 72.5.)

Fig. 10.—Cystic renal corpuscle with obvious glomerular tuft and thickened arteriole, attached to a short proximal tubule which terminates in a cyst (Case 6). (× 81.) Renal corpuscle, 446 × 250 μ; tubule diameters range, 25-50 μ; cyst, 310 × 235 μ.
Case 1 there were regions where a few isolated cystic tubules existed in large expanses of connective tissue. In other cases (Nos. 2, 5, and 6) there was quite remarkable reduction of the parenchyma, but many of the medullary tubules exhibited active hyperplasia of the cell linings (Case 6). In these instances the medulla was reduced to a few cystic elements or sometimes only minute structures were present (Cases 1, 2, 5, and 6).

Scattered areas of haemorrhage were present (Cases 1, 2, and 4) and cellular infiltrations were seen in all cases. The latter consisted mainly of small round cells but included plasma cells, occasional polymorphonuclear leucocytes, macrophages, and numerous fibroblasts.

(d) Blood Vessels.—Some of the vessels were thin walled and sinusoid in character (Case 5) but many showed medial thickening (Cases 4, 5, and 6).

Microdissection Studies. Examination of tissue during microdissection provides evidence of topographical and spatial relations not available by other means. The emphasis on smaller cysts in histological studies applies, in considerable measure, here also. However, since it is the smaller examples that are closest to normal structures, both in their own architecture, with preservation, at least in part, of the glomerular tuft, and in the relation and frequent attachment to the tubular system, this has significant advantages. The various forms of small cysts, with their clear gradations to the larger ones, provide reasonable presumptive evidence of the mode of development of this group from the normal corpuscle. Moreover, during dissection the intermediate-sized cysts are visualized even though their precise topographical relations and connexions are not recognizable.

The smallest cysts are slightly dilated corpuscles (Figs. 3 and 4); there are all gradations between these and large, even colossal, cysts (Fig. 5). The degree of distension is apparent when we consider that the diameter (in figures) is related to the cube root of the cyst volume. A cyst twice the diameter is eight times the size of the normal renal corpuscle.

In the small cysts a glomerular tuft is clearly distinguishable. Its size varies considerably (Figs. 6 and 7); in the smallest, whose diameter exceeds that of the normal corpuscle only slightly, it may occupy most of the cavity (Fig. 8). With increasing cyst size, the relative volume of the tuft becomes less and even disproportionately so and gradually disappears (Fig. 9). Though usually single, it or its remnants may be double or multiple. The larger cysts are morphologically indistinguishable from others, and this is where microdissection is specially valuable in demonstrating topographical relations and connexions with the tubules and blood vessels.

The wall of the cyst is thin but it becomes thicker with enlargement and, presumably, with increasing age. Often the large cysts collapse and become more or less crenated and folded.

The distribution of the cysts conforms with that already mentioned above. They occur in the cortex and are usually more numerous in the subcapsular zone. During dissection, cysts and cyst groups become separated from the tissue mass as the superficial tissue is removed. In the foetus they are associated with groups of developing corpuscles (Case 3).

A communication with the proximal convolution is found in most of the small cysts. Larger cysts have a much narrower connexion (Fig. 5). In accordance with a general phenomenon, the larger the cyst the smaller and more delicate this junction. As the cyst enlarges, the link becomes elongate and tenuous. In still larger cysts no communication is found.

The proximal convolution, with which the cyst communicates, may be part of a complete nephron, but, at times, atrophy of parts of the tubule has occurred leaving only residual segments, and the cyst then communicates with a short blindly-ending loop of the tubule or may terminate in a cyst (Fig. 10).

The blood vessels supplying the small cysts correspond closely with those of the normal corpuscle and this usually applies to cysts retaining a tuft or tuft remnants. Frequently the efferent vessel is considerably thickened and is often of dimensions comparable with the afferent arteriole, which demonstrates, at times, an obvious vessel of Ludwig. In larger examples the blood supply of the wall is less clearly defined and does not approximate to any normal blood supply of the corpuscle.

Changes in the Tubules. The two normal forms of nephron, the long loop and short loop, are found, but in most cases the difference between these is greater than usual (Cases 3, 4, and 6; Fig. 11).

Changes in a nephron may be of two kinds, occurring separately or together.

(i) Dilatation occurs either along the whole or most of the tubule, to a different degree in different parts, or as a single swelling or multiple localized distensions in different parts, constituting cysts. These may be few in number or, infrequently, numerically equal to the corpuscular type cysts (Case 6).

Their tubular character and origin is apparent when they are part of, and continuous with, the tubule. With enlargement, as in the case of the corpuscular cysts, their attachment may become
smaller until this is a stalk which is elongate and thin. This gradually withers and disappears. At this stage the origin of the cyst becomes indeterminate.

Associated with the enlargement of the tubule or part of it there is an increase in the number of lining cells. It is apparent that some hyperplasia of parenchymal elements must have occurred. These localized areas of hyperplasia may be associated with the production of numerous diverticula (Fig. 12).

(ii) Atrophy of parts of the tubule is demonstrated by the occurrence of blindly-ending tubular segments separated from adjacent portions of the same nephron. Sometimes almost the whole nephron has disappeared (Cases 1, 3, 4, and 6).

Corpuscles and small cysts communicate with short (Fig. 13) (or long) segments of the proximal convolution. This segment may have a normal diameter or may be dilated.

Fig. 8.—Enlarged renal corpuscle, $470 \times 350 \mu$ (reniform shape), with a thickened efferent arteriole branching to neighbouring coils of a proximal convoluted tubule (Case 2). ($\times 140.$)

Fig. 9.—Diagrammatic representation of the range of cyst size observed in Case 4. (A) represents a normal renal corpuscle, (B-E) the range of cysts (without tubular connexions).

Fig. 10.—Diagrammatic representation of (A) normal long loop nephron and (B) corresponding nephron from Case 4. The abnormal nephron shows a cystic renal corpuscle and dilatation of all tubular elements as well as an increase in length.
On the other hand, occasional aglomerular nephrons or segments were found, showing that atrophy also affects some of the corpuscles (Cases 1, 3, and 6).

**Discussion**

It has long been thought that cysts arise in some part of the nephron and that different parts can be involved. However, it is only relatively recently that reasonably precise information has been available and, even yet, this is small in amount. Cysts of the corpuscle or the tubule are recognized, but much more detailed knowledge is required.

The gross appearances and the distribution of cysts are commonly so similar in different types that distinction can be made only on histological study. Moreover, it is in only a proportion (the smaller and early forms) that significant differences are found.

When these have been established it is then possible to recognize differentiating features in some previously indeterminate types and to suggest the probable
Similar changes occur in the tubules. Dilatation and hyperplasia may be diffuse or localized to certain parts of the nephron. Not unnaturally, such changes are more obvious in cases where tubule irregularities are comparable in degree with those of the corpuscle (as in the typical mixed type of cysts—Case 6) than in predominantly corpuscular cystic organs. These tubular cysts appear to fall into groups according to the specific region especially involved, but this question belongs more properly to the consideration of tubular cysts. What is important is that cysts may be localized to one zone and that tubules of normal diameter may be present above and below the cyst.

Atrophy and hypoplasia also occur. Parts of the nephron shrink and disappear. This leaves incomplete units, with blind ends, and these may be dilated (or even cystic) or may be normal in diameter. At other times the unit may terminate in a diverticulum or a connective tissue tuft.

The corpuscle or cyst is therefore in communication with either a complete nephron or a short blindly-ending portion of the proximal convolution or longer nephron component. Where this is grossly distended, the corpuscle or cyst communicates with a tubular cyst. More frequently, however, there is a thin tubule uniting the corpuscular cyst with another cyst lower down in the nephron. This has an important bearing on the explanation of the mode of development of these renal cysts.

The hypotheses proposed fall into two main groups:

(i) The older ones, in general, have a fundamentally mechanical basis. Obstruction to some part of the tubule, due to inflammation, with stricture development or compression, or to a 'failure of union' of the nephrogenic zone, with the outgrowth from the Wolffian duct, implies a localized area above which dilatation should occur. The localization of cysts to one region, such as the crest of Henle's loop, and the normal tubule between this and the corpuscle shows that the simple hypothesis depending, presumably, on hydrodynamic factors alone is quite inadequate.

(ii) Recent investigations show that the factors responsible are usually of another (chemical) kind and are much more complex than was originally envisaged. Not only has the importance of metallic ions been shown to be significant in the adult, but the concept of complex chemical substances (organizers) in the foetus has opened up a new field. In addition, there are indications that tissue inter-relations, with the action of physicochemical or physical factors, also play an important role.

These factors are still insufficiently understood to
allow us to allocate any specific processes to these tissue changes, but the maintenance of an organoid and complicated structure in itself demonstrates the complexity of the factors involved. At the same time, this alters our outlook and enables us to assess critically the mechanical views that have imposed unsubstantiated philosophical notions on morphology and pathology.

Thus, though we begin simply with a study of the structural features of these cysts, this provides information that has an important bearing on concepts of cyst development.

Conclusions

Cysts of corpussular type and form comprise a group that can be distinguished from tubular cysts.

In a series of 25 cases, they constituted almost a quarter (6 cases). In this group, corpussular cysts usually predominate (5 cases) but were found to be mingled with an equal number of tubular cysts in one case (Case 6). They occur in the cortex and may predominate in the subcapsular zone.

Small cysts contain tufts or tuft remnants and are often still attached to the proximal convoluted tubule. Larger cysts may be recognizable by their relation to the tubule or association with undoubted corpussular cysts; but still larger ones are usually indistinguishable from the larger tubular cysts.

Changes are found also in the tubules. Diffuse or localized dilatations accompanied by hyperplasia occur and cysts are found along the tubule. Localized areas of hyperplasia may result in the formation of diverticula.

Retgressive changes are also associated with the proliferative activity. Corpusses disappear and agglomerular nephrons are seen. Atrophy of parts of the tubules results in incomplete segments of different parts of the nephron.

These observations show that mechanical factors, implicit in older hypotheses (such as, for example, the ‘failure of union’ proposition), are insufficient to explain the data. The cysts develop from the action of complex factors which, though producing maximal effects at certain sites, affect the tissue as a whole.

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