Renal Disease

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Preface

Any book should have a purpose; and it should be possible to state it, even if the statement is approached obliquely, by way of negatives. This is not an elementary book on renal disease; nor is it a comprehensive advanced text-book, for this would not be possible in a single volume, if at all. The underlying intention, as was explained to contributors at the beginning, is to indicate the present views, and to some extent the outlook, of men who have made significant contributions to various aspects of our knowledge of renal disease.

How then does it differ from the ubiquitous reports of symposia, which are also selective in their authorship, multi-disciplinary in their approach, and not devoid of speculation on future trends. It is more ambitious in concept, with a view to its being more permanent in appeal. The essence of a symposium is its informality, and this tends to be all too faithfully reflected in the opening papers, which are often hurried, contrived and otiose. In this book, time was allowed for a more thoughtful approach, and I think this is apparent in the quality of the contributions. The present time is not devoid of excitement, in renal studies as elsewhere, and this is obvious in many of the chapters.

The success of an enterprise like this depends on the efforts of the contributors. I have been very fortunate in that almost all of those whom I first approached consented to undertake this additional heavy commitment. Having chosen my team carefully, and, I hope, indoctrinated them subtly, I have tried not to be a fussy editor.

When a large subject is looked at from different points of view, some degree of overlap is inevitable, if each contribution is to be coherent. What I have tried to do is to avoid the duplication of extended accounts of any single topic; but I have not excluded brief accounts of conditions in a special context, e.g. radiology, because there is a more definitive account elsewhere. Where my contributors have held conflicting opinions — and this could be avoided only by having contributors who held no opinions — I have let each state his case, and not presumed to resolve their differences. What is thereby lost in artificial consistency should be gained in accurate representation of where the problems lie.

The chapters fall into three broad groups — basic information; 'natural history' and methods of investigation; and relationships between renal disease and general medicine. These are not rigid divisions, but cross-reference should be made easier by the short list of contents which precedes each chapter, as well as by the index.

While my main debt is to those who have written the book, I must also express my thanks to my colleagues Sir Robert Platt and Dr S. W. Stanbury, with whom I have discussed the project at various stages; to Mr Per Saugman, of Blackwell Scientific Publications, who both started me off and kept me going; to Dr Robert Ollerenshaw and his staff for help with the illustrations; and to my secretaries Mrs J. Butler and Miss H. M. Souva for successively taking on this extra burden.

D. A. K. BLACK

Contents

PART 1

CHAPTER 1

The Anatomy of the Human Kidney

Introduction

The kidneys are paired organs which lie behind the peritoneum of the posterior abdominal wall. Each kidney measures some $12 \times 7 \times 3$ cm and weighs 120 to 170 g. The medial aspect of the kidney shows an indentation, the hilum, through which pass the major renal blood vessels and the pelvis of the ureter. In the cadaver the hilum usually lies opposite the upper part of the body of L2 vertebra while the upper and lower poles of the organ reach the bodies of T12 and L3 vertebrae respectively. In life the position of the organ varies with posture (Moody & van Nuyes, 1940) and respiration (Tchaperoff, 1938): the normal excursion between deep inspiration and expiration being approximately one vertebral body. According to Smith, McKim & Rush (1936) a respiratory movement of more than 2·5 cm is abnormal. The upper poles of the kidneys lie nearer the mid-line than the lower poles owing to the presence and contour of the adjacent psoas major muscle. Relative to the skin of the back, each kidney lies obliquely in the rectangle (of Morris) made by drawing vertical lines 2·5 cm and 8·75 cm from the mid-line and two horizontal lines through the spines of T11 and L3 vertebrae.

In some cases, possibly because of the mass of the liver on the right side of the abdomen, the various parts of the right kidney lie 1·25 cm to 2·5 cm caudal to the corresponding parts of the left organ.

Renal Fascia

A condensation of retroperitoneal connective tissue, usually referred to as the renal fascia, surrounds each kidney and the adjacent adrenal gland. Its density varies markedly in different individuals. The renal fascia may be arbitrarily divided into anterior and posterior layers which fuse with each other above the adrenal gland and lateral to the kidney. On the medial aspect of the upper pole of the kidney the two layers are also continuous, but opposite the hilum the posterior layer blends with both the fascia over the psoas major and that surrounding the ureter and renal vessels (Martin, 1943), while the anterior layer is continuous with a condensation on the anterior aspect of the renal vessels and hence

is theoretically continuous across the mid-line with the fascia of the opposite side. According to Tobin (1944) the anterior and posterior layers only fuse with the walls of the renal pelvis and blood vessels after birth and in the foetus there is a direct communication between the fascial spaces of the two sides. The posterior layer of renal fascia is quite separate from the fascia transversalis. In adult specimens the two layers of fascia are usually lost below the kidney in the general mass of retroperitoneal connective tissue. Though both the adrenal gland and kidney are enclosed in the same fascial envelope the two are separated from each other by a connective tissue septum which runs obliquely from the anterior to the posterior layer of the renal fascia. The retroperitoneal tissue adjacent to the kidney contains a variable quantity of fat which tends to increase in amount with age. The term perirenal fat is applied to any adipose tissue lying within the renal fascia while fat lying outside this structure is known as pararenal fat.

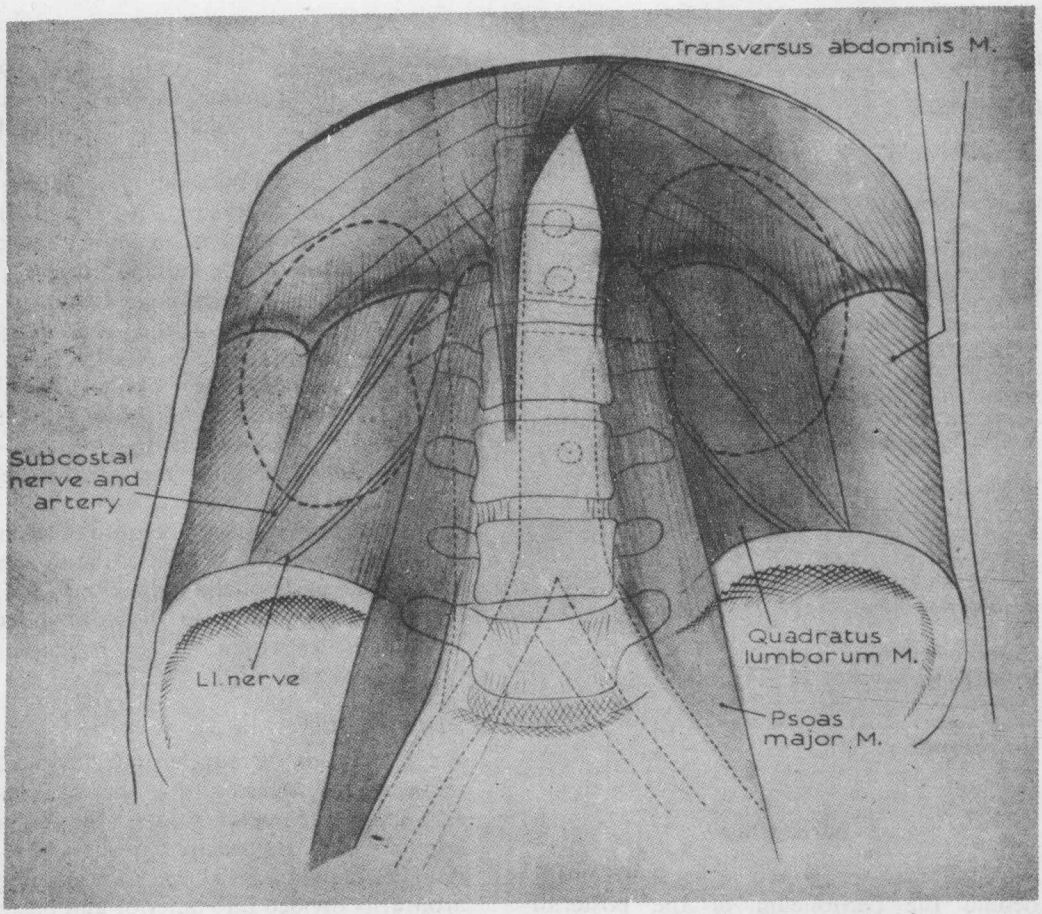

FIG. 1.1. Posterior abdominal wall showing outline of kidneys, vertebrae and major blood vessels.

Relations of the Kidney

Posterior Relations

Both kidneys are related posteriorly to the diaphragm, the lateral and medial lumbo-costal arches, and to the psoas major, quadratus lumborum and transversus abdominis muscles (Fig. 1.1). A variable amount of fibro-fatty tissue which includes the renal fascia, peri- and pararenal fat and fascia transversalis intervenes between the kidney and these muscles. At the junction of the lateral and medial lumbar-costal arches, the tip of the transverse process of the first lumbar vertebra is in close proximity to the organ. The left kidney commonly extends cranially as far as the shaft of the eleventh rib while the right organ may only reach as far as the upper border of the twelfth rib, hence the left kidney may have a more extensive relationship with the pleural cavity. The subcostal nerves and vessels and the first lumbar nerve are close relations of the posterior surface of both organs. The subcostal nerve appears under the lateral lumbo-costal arch and then crosses the anterior surface of the quadratus lumborum, running on a line which extends from the tip of the transverse process of L1 to the infero-lateral angle of the quadratus lumborum. The first lumbar nerve appears at the lateral border of the psoas major approximately mid-way between the transverse processes of the L1 and L2 and runs from this point downwards and laterally parallel to the subcostal nerve. The subcostal vessels lie supero-lateral to the corresponding nerve. These nerves and vessels are bound down to the sheath of the quadratus lumborum by a continuation of the fascia transversalis.

More distant posterior relations (Fig. 1.2) are the sacro-spinalis and associated lumbar fascia, the serratus posterior inferior, latissimus dorsi and often part of the internal oblique. The organ is, therefore, related to the Superior Lumbar Space (Grynfeltt's), bounded medially by the lateral border of the sacro-spinalis, superiorly by the lower border of the serratus posterior inferior and twelfth rib and infero-laterally by the posterior border of internal oblique. The floor of the space is formed by lumbar fascia from which the internal oblique takes a variable origin.

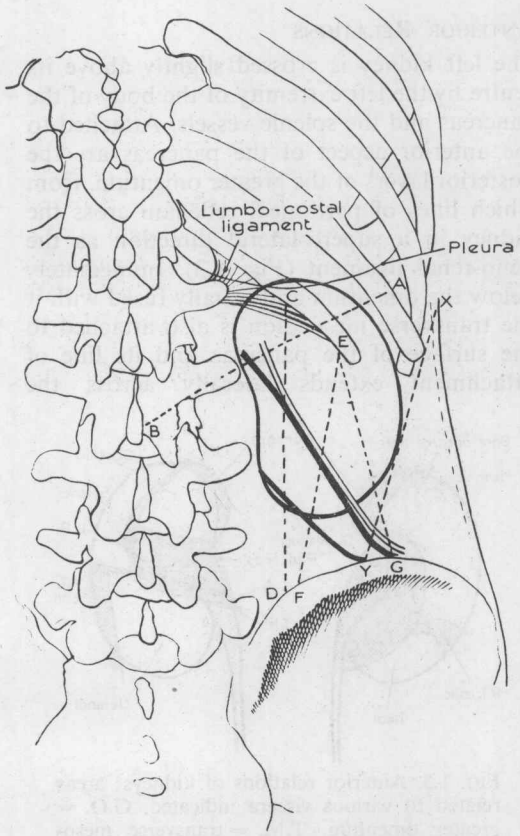

FIG. 1.2. Distant posterior relations of right kidney. Position of subcostal and first lumbar nerves indicated. AB = lower border of serratus posterior inferior muscle. CD = outer border of sacrospinalis. EF = posterior border of internal oblique muscle. EG = posterior border of external oblique muscle. XY = anterior border of latissimus dorsi muscle.

Superior Relations

Each kidney is related to an adrenal gland which extends for some distance on to the

medial aspect of the organ. The two structures are separated by a septum of renal fascia.

Anterior Relations

The left kidney is crossed slightly above its centre by the left extremity of the body of the pancreas and the splenic vessels. Attached to the anterior aspect of the pancreas are the posterior layers of the greater omentum, from which lines of peritoneal reflexion cross the kidney in a supero-lateral direction as the lieno-renal ligament (Fig. 1.3). Immediately below the omentum and usually fused with it the transverse mesocolon is also attached to the surface of the pancreas and its line of attachment extends laterally across the

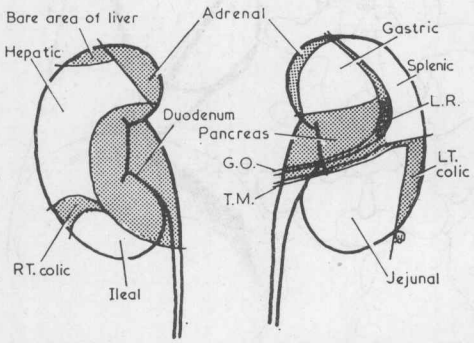

FIG. 1.3. Anterior relations of kidneys; areas related to various viscera indicated. G.O. = greater omentum, T.M. = transverse mesocolon, L.R. = lienorenal ligament.

kidney to the bare area for the descending colon. Above the pancreatic area the kidney is covered by peritoneum of the lesser sac and is related to the posterior surface of the stomach. Lateral to the lieno-renal ligament the organ is covered by peritoneum of the greater sac and is related to the spleen. The lower pole of the organ on its antero-medial aspect is covered by peritoneum of the greater sac and is related to coils of the jejunum.

The upper part of the anterior aspect of the right kidney (Fig. 1.3) is related to the bare area of the liver while the second part of the duodenum covers the medial part of the organ. The lower half of the anterior surface is crossed by the terminal part of the ascending colon and right colic flexure. Peritoneum covers the anterior surface of the organ over its central and lateral parts and this portion of the kidney forms part of the floor of the renal well (of Morison). A small area near the lower pole of the organ is also covered by peritoneum and is related to the coils of the ileum.

General Structure of the Kidney

The external aspect of the kidney presents a smooth surface covered by the renal capsule. The anterior and posterior surfaces, upper and lower poles and the lateral margin have a convex contour while the medial margin is concave due to the presence of the hilum. Through the hilum of the kidney, the main blood vessels, renal pelvis and nerves pass to

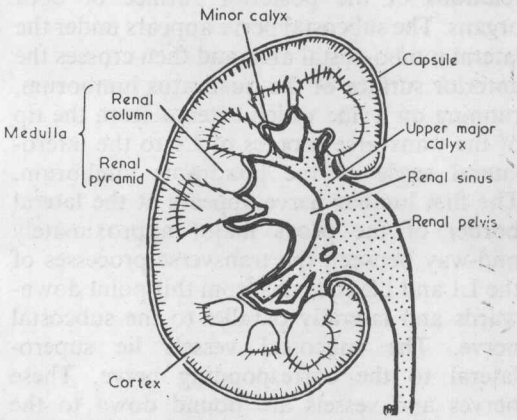

FIG. 1.4. Longitudinal section through kidney showing cortex, pyramids, renal sinus, renal pelvis and calyces.

enter a space, the renal sinus (Fig. 1.4). The renal parenchyma bordering the sinus is covered by renal capsule except where the minor calyces cap the renal papillae. The contents of the renal sinus include blood vessels, nerves, renal pelvis and a variable amount of adipose connective tissue. If the organ is bisected longitudinally its cut surface

shows two distinct regions, the cortex and medulla. The medulla is composed of two functionally and structurally distinct elements, the renal pyramids (pyramids of Malpighi) and the renal columns (columns of Bertin); the latter are continuous with the renal cortex. Each renal pyramid presents an external basal region which lies in the boundary zone of the kidney and an apex which projects as a renal papilla into the renal sinus. Pyramids converge as they pass towards the sinus and two or more may share a single papilla (Maresch, 1896). In consequence of this fact and also the fact that two or more papillae may open into a minor calyx the relative numbers of minor calyces: papillae: pyramids are in the order of 1:2:3 though the gradient may be even greater.

The Renal Pelvis and Calyces

In the immediate vicinity of the kidney the upper end of the ureter usually dilates to form the renal pelvis. This is a funnel-shaped structure which enters the renal sinus before dividing into two, or less commonly, three sessile or pedunculated tubes, the major calyces (Fig. 1.4); these in turn divide into a variable number (8-14) of minor calyces. The minor calyces are invaginated by the renal papillae and the epithelium which lines the calyces is directly continuous with that of the collecting tubules. The external fibrous layer of each minor calyx fuses with the renal capsule. In some cases, the pelvis is absent and the ureter divides without dilatation into two or more major calyces. The point of division of the renal pelvis (or ureter when the pelvis is absent), varies and in some cases the major calyces are formed outside the renal sinus and pass through the hilum to enter this structure. The relation of the various forms of renal pelvis to the flow of urine was considered in detail by Rose, Hamm, Moore & Wilson (1933) who classified them into two main types, a dysuric type from which flow is impeded and a non-dysuric type in which free flow occurs.

Embryology

Since the work of Felix (1906) it has often been assumed that the human kidney develops in three successive and distinct phases which differ from each other temporally, spacially, structurally and phylogenetically. The organs are referred to as the pronephros, mesonephros and metanephros. Supporters of this concept believe that the pronephros exists as a functioning kidney only in the lowest vertebrates and their larvae, that the mesonephros is the functional kidney of amphibia while in amniotes (reptiles, birds and mammals) the metanephros is the definitive organ. An alternative view has, however, existed since the work of Price (1897) and according to this all parts of the excretory system form a single unit, the holonephros. Comparative work recently reviewed in detail by Frazer (1950) is in keeping with this latter concept. It is apparent from Frazer's work that there is no clear-cut distinction between the structure of the pronephros and mesonephros in certain forms and that even in fishes the more caudal tubules may show a tendency to separate from the remainder of the kidney and form an isolated metanephros. The terms pronephros, mesonephros and metanephros may, however, be conveniently retained in order to indicate the relative position of renal tubules in a particular animal. In mammals the pronephros is cervico-dorsal, the mesonephros dorso-lumbar and the metanephros initially sacral in position.

The Pronephros

In man the holonephros develops from the mesoderm of the nephrogenic portion of the intermediate cell mass. The more cranial portions are the first to differentiate and form tubules, but these are rudimentary. Differentiation then proceeds in a cranio-caudal direction and the more caudal tubules persist into adult life as the functional kidney (metanephros). According to Torrey (1954) a few nephrotomes appear transitorily over the first six somites, but play no part in the

formation of the organ. From the seventh somite caudally a nephrogenic cord is elaborated, the most rostral part being rudimentary. An excretory channel, the primitive nephric or Wolffian duct, appears independently of the pronephric nephrons at the level of the ninth somite (Torrey, 1954). From this point to the fourteenth somite the duct develops segmentally by delamination from the local mesoderm. In this way a cord of cells is formed and its tip then grows caudally independent of local mesoderm and according to Shikinami (1926) reaches the cloaca at the 26- to 28-somite stage (4 weeks). The cord is not, however, canalized until the 26-somite stage. In man, though some 7 pairs of rudimentary pronephric tubules may be recognized, they rarely canalize and the rostral tubules begin to disintegrate before the more caudal ones differentiate.

The Mesonephros

In the 3 mm embryo mesodermal condensations are apparent in the nephrogenic portion of the intermediate cell mass in the thoracic region and form the mesonephric part of the organ. The process commences rostrally and gradually extends towards the tail end of the embryo. Cord-like cellular condensations appear and later canalize. The lateral extremities of the cords fuse with the pre-existing Wolffian duct while the medial extremity of each cord becomes thinned out and invaginated by a glomerular tuft of capillaries; the composite structure being a Malpighian corpuscle. The mesonephric tubules elongate and become convoluted. In the 7 mm embryo mesonephric tubules extend caudally as far as the third lumbar segment, and at this stage some 32 mesonephric tubules may be recognized. Degeneration of the cranial mesonephric tubules begins in the 5-6 mm embryo at a time when the caudal tubules are still developing. A wave of degeneration extends caudally and is usually completed by the 21 mm stage. Degenerative changes affect the Malpighian corpuscles and a proportion of the tubules, but some cranial and caudal tubules persist. The cranial ones become associated with the developing gonads to form the conducting tubules (efferent ductules) of the male genital system while others remain as the appendix of the epididymis, paradidymis, and aberrant ductules. In the female the tubules persist as the epoöphoron and paroöphoron.

The Metanephros

The part of the holonephros which lies caudal to the third lumbar segment and extends down into the future pelvis is the last to develop and forms the metanephros.

Differentiation of the Ureteric Bud

The primitive nephric duct can be traced down the lateral aspect of the urogenital fold and in the 17 mm embryo and older specimens it lies dorsal to the Müllerian duct in an elevation known as the tubal ridge. The lower end of the duct can be traced initially into the cloaca and subsequent to the formation of the cloacal septum into the urogenital sinus. Shortly before its termination the nephric duct makes an acute bend from which at the 3 mm stage (horizon XV Streeter) the ureteric bud arises. The ureteric bud grows at first dorsally and then rostrally to enter the lower end of the nephrogenic cord. The distal

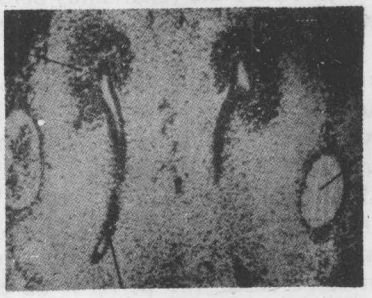

FIG. 1.5. Section through the pelvis of a 10 mm human embryo showing ureteric buds and metanephrogenic caps (×90 reduced to ⅓).

extremity of the bud expands to form a primitive renal pelvis and in its vicinity a mesodermal condensation, the metanephric blastema, forms (Fig. 1.5). As the ureteric bud elongates the primitive renal pelvis together with the associated metanephrogenic mesoderm is carried cranially and ascends the posterior abdominal wall dorsal to the remains of the mesonephros. The two metanephric blastemata are initially closely approximated as they lie in the pelvis and may be in physical contact with each other. They are flanked laterally by the umbilical arteries (Fig. 1.5). This close association is particularly well displayed in 8-10 mm embryos. The metanephros reaches its definitive position at the level of the second lumbar segment in the 16 mm embryo. The ascent may result in part from the elongation of the ureteric bud, but is at least partly due to the concomitant development and elongation of the whole hind end of the embryo.

The primitive renal pelvis becomes dorsoventrally flattened at an early stage and develops distinct cranial and caudal poles. From each of these poles and from the intermediate zone between the two poles, primary tubules grow out into the metanephrogenic tissue (Fig. 1.6). From these primary tubules a succession of generations of tubules arise and give rise to the 'ureteric trees' (Felix, 1912): the trunks of these are the primary tubules. As the tubules extend into the metanephrogenic tissue they carry with them condensations of mesoderm. The tubules together with the associated metanephrogenic mesoderm form a number of pyramidal masses of tissue which give the developing organ a lobulated character. Nephrogenic tissue not only covers the tubules at their peripheral extremities, but also extends for some distance along the sides of these elements towards the centre of the developing organ and adjacent metanephrogenic caps are, therefore, in contact with each other. Adjacent parts of lobules persist in the adult as the renal columns of Bertin though the surface lobulation of the organ normally disappears shortly after birth, due to growth of the peripheral cortex. The cavity of the primitive pelvis eventually remains as the definitive renal pelvis, the primary tubules remain as the major calyces, the secondary tubules as the minor calyces. According to

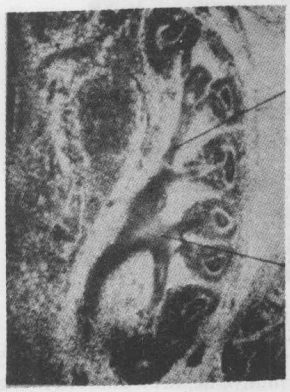

FIG. 1.6. Section through metanephros of 15 mm human embryo showing primitive renal pelvis, primary and secondary tubules and metanephrogenic caps (×90 reduced to ⅓).

Felix absorption of tubules of the third and fourth orders occurs in embryos of approximately 60 mm in length, so that eventually the fifth order tubules, which remain as papillary ducts, are left opening directly into the minor calyces.

Development of Nephrons

The presence of the ureteric bud and its derivatives, the primitive tubules, in contiguity with the metanephrogenic blastema results in the induction of nephron formation in the metanephrogenic tissue (Brown, 1931; Boyden, 1932; Gruenwald, 1939). Initially a condensation of mesoderm appears adjacent to the terminal buds of the various orders of collecting (ureteric) tubules. These condensations later become vesicles which finally elongate to form the metanephric tubules. Individual nephrons elongate and become convoluted. The distal extremities of these structures make contact with the collecting

(ureteric) tubules (Fig. 1.7) and later fuse with them. At a still later stage the lumina of nephrons and collecting elements become continuous.

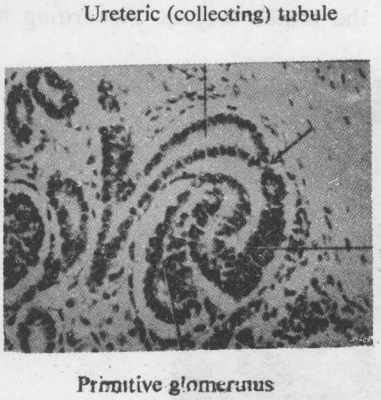

FIG. 1.7. Section through metanephros of 55 mm foetus. A primitive nephron and collecting tubule have established contact at point indicated by arrow, but union has not occurred (×350 reduced to ½).

While the metanephric tubules are elongating and establishing contact with the collecting elements the proximal end of each tubule becomes thinned on one side, the cells becoming squamous. In the mesoderm adjacent to this layer of flattened cells vascular spaces appear and invaginate the thinned wall of the tubule (Fig. 1.7). The vascular channels persist as the glomerular capillaries, while the squamous cells form the visceral and parietal layers of Bowman's capsule. The whole structure forms the Malpighian corpuscle.

The part of the nephron between the Malpighian corpuscle and the point where it joins the collecting tubule elongates rapidly and at an early stage two distinct regions can be identified: these will develop into proximal (Fig. 1.8) and distal convoluted tubules. The coils of the convoluted tubules initially lie external to their Malpighian corpuscles; as development proceeds, however, each nephric tubule elongates and the mid-part extends towards the centre of the organ as a distinct 'U'-shaped loop — the loop of Henle. The cells forming the wall of this loop initially resemble those of the convoluted elements.

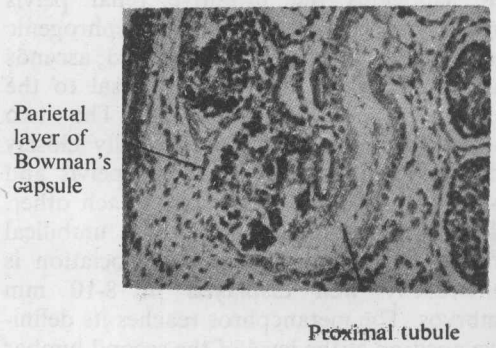

FIG. 1.8. Section through developing metanephric tubule of a 55 mm foetus showing Malpighian corpuscle and proximal tubule (×300 reduced to ½).

In foetuses of 92 mm, however, a thin segment is apparent (Fig. 1.9) and this subsequently elongates.

The radial growth of the ureteric tubules

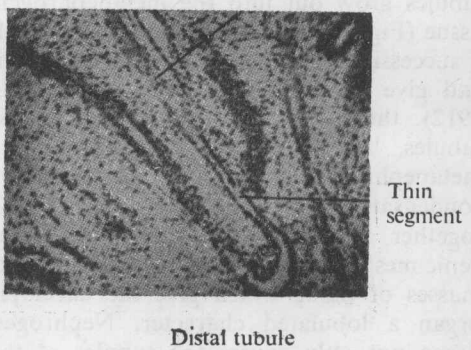

FIG. 1.9. Section through metanephros in a 92 mm foetus showing formation of the thin segment of loop of Henle (×170 reduced to ½).

and the addition of metanephric tubules at the periphery, results in the formation of an organ in which the more central elements are older than those near the surface. This

method of growth necessitates some change in the initial sites of opening of the earlier generations of collecting tubules. According to Kampmeier (1923, 1926) the metanephric tubules associated with primary and secondary collecting (ureteric) tubules degenerate in whole or part during foetal life. The writer's findings in foetuses of 55, 94, 142 and 155 mm C.R. length are in keeping with this view. In all these specimens collapsed and degenerating tubules have been observed in the more central part of the organ. In 94 and 142 mm specimens, distended (cystic) tubules and degenerating Malpighian corpuscles were also observed (Fig. 1.10). Cystic changes presumably occur when the lumen of tubules is blocked before cessation of glomerular function.

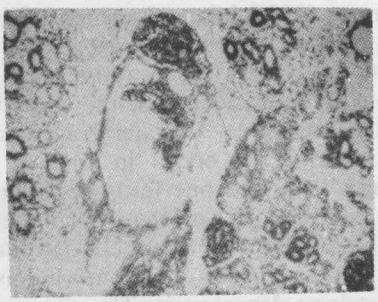

FIG. 1.10. Cystic degenerating nephron in a 142 mm foetus. The glomerulus is markedly atrophic (×140 reduced to ½).

According to Vimtrup (1928) and Moore (1931) each normal adult human kidney contains approximately one million glomeruli and there is no appreciable nephrogenesis after birth. Post-natal increase in renal volume is the result of the maturation of glomeruli (which may not reach full maturity until 3-12 years of age) (Torrey, 1954), to the increase in length and diameter of the various tubules, and to the concomitant increase in nervous, vascular and supporting connective tissue elements.

Malpighian corpuscles show a considerable variation in size during different developmental stages. The transient structures associated with the primary and secondary ureteric tubules have a similar diameter to those of the adult organ. The later (permanent) corpuscles are, however, considerably smaller during foetal life and many only reach full size after birth (MacDonald & Emery, 1959).

Although a kidney which is solitary, either congenitally or after operation, is known to increase in size, there is no evidence that the enlargement is due to an increase in the number of nephrons (Moore, 1929, 1930a; Jackson & Shields, 1927).

When the ureteric bud first makes contact with metanephrogenic tissue the primitive ureteric pelvis is associated with the ventral or anterior face of the organ. As observed by Weyrauch (1939), a ventral pelvis still exists in 12·5 mm embryos. Rotation subsequently occurs and in a 19·5 mm embryo the pelvis is ventro-medial (Fig. 1.11) while in 40 mm and

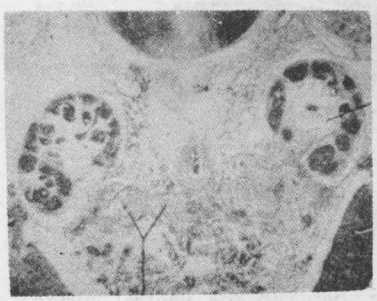

FIG. 1.11. Section through metanephroi of a 19·5 mm embryo. Note ventromedial position of the hila and developing para-aortic chromaffin bodies lying between the kidneys and the central aorta (×60 reduced to ½).

older specimens it normally enters the medial side of the organ. Developing extra-adrenal chromaffin bodies form a prominent feature of sections through the organ at the 19·5 mm stage (Fig. 1.11). Some of these subsequently persist in association with the fibres of the renal sympathetic plexus (Coupland, 1952, 1954).

Development of Blood Vessels

The Renal Arteries. Felix (1912) gave a detailed description of the blood supply of the human kidney and the main essentials of this work can be confirmed in 8-19·5 mm embryos. During early embryonic life a series of non-segmental lateral splanchnic arteries pass from the aorta to the mesonephros and adjacent intermediate-cell-mass derivatives. The vessels were divided by Felix into three groups: a cranial group of two arteries which pass dorsal to the adrenal gland, a middle group of two or three which pass through the adrenal, and a caudal group passing ventral or caudal to the adrenal and comprising four or five vessels (Fig. 1.12). The lower group of vessels forms a plexus, the rete

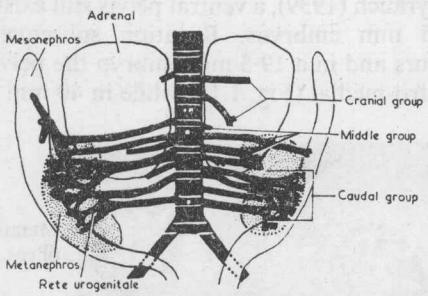

FIG. 1.12. Mesonephric arteries and rete urogenitale; vertebral levels indicated (after Felix, 1912).

urogenitale, between the ventral surface of the developing metanephros and the dorsal aspect of the gonad. Initially each organ is supplied by a number of vessels which may either arise from the mesonephric arteries or from the urogenital rete. The subsequent degeneration of some vessels and enlargement of others results in the persistence of particular channels which remain as adrenal, renal or gonadal arteries. According to Felix the definitive renal artery is usually the remains of the last vessel of the middle group or the first of the caudal set. The main channel is already clearly distinguishable in 46 mm foetuses.

The Renal Veins. The definitive renal veins are derived in large part from the remains of the supracardinal-subcardinal venous anastomosis. The left opens into the subcardinal portion of the inferior vena cava while the right opens into the supracardinal-subcardinal portion. In consequence the renal veins normally lie anterior to the aorta and renal arteries.

Congenital Abnormalities

The kidney not infrequently exhibits congenital anomalies, some of which can be ascribed to errors at specific developmental stages. These will be considered briefly.

Renal Agenesis

Agenesis may be unilateral or bilateral, the latter being incompatible with life. According to Soloway (1939) bilateral agenesis occurs in one in 6000 neo-natal autopsies. Since, however, not all cases reach full-term, a true estimate of the incidence of the condition is virtually impossible. Unilateral agenesis has been reported to occur in one in 1817 (Anders, 1910) and one in 1444 (Campbell, 1928) routine post-mortem examinations, while Maluf, Ford & Spurr (1947) found an incidence of one in 500 of 2000 new admissions to a urology department. The observations of Nicholson (1927) and the descriptive and experimental work of Brown (1931), Boyden, (1932) and Gruenwald, (1938, 1939) suggest that the presence of a normal ureteric bud is essential for the induction of metanephric tubules and hence some cases of agenesis may be due primarily to an absence of this outgrowth. Such cases would also show a total absence of the ureter on the affected side. Collins (1932), however, in a review of 572 cases of congenital unilateral renal agenesis reported that the ureter was totally absent in only 51 per cent of cases. Some of these cases of so-called agenesis may, therefore, have been extreme examples of hypoplasia, while others may have resulted from an abnormality of intermediate-cell-mass mesoderm

with agenesis of the metanephric part of the holonephros. In the majority of cases a more widespread agenesis of intermediate-cell-mass mesoderm was excluded by Collins's finding that the ipsilateral adrenal was only absent in 11 per cent of cases, while the testes and ovaries were absent in less than 2 per cent and 4 per cent of cases respectively. A case of congenital solitary kidney with crossed ureter, reputed to be the fifth in the literature, was reported by Alexander, King & Fromm (1950). One possible cause of this latter anomaly may be unilateral agenesis of the ureteric bud with agenesis of the caudal part of the contralateral holonephros. In unilateral agenesis the solitary kidney contains a normal number (approx. one million) of glomeruli (Moore, 1930b).

Renal Hypoplasia

Hypoplasia may be unilateral or bilateral. According to Murray & Sandison (1941) bilateral cases are uncommon. Since the ureter of the affected kidney is usually hypoplastic in these cases, an abnormal ureteric bud may be the primary cause of the anomaly. Johnson & Wayman (1936) found that hypoplastic kidneys contained fewer glomeruli than normal. In some cases the renal parenchyma is grossly reduced and cartilage is present (Bigler & Killingsworth, 1949), while in other cases primitive glomeruli or tubules may co-exist (Arnold, 1960).

Supernumerary Kidney

Such kidneys are usually also ectopic and smaller than normal. Carlson (1950) reviewed fifty-one cases. The abnormality results from an abnormal division of the ureteric bud and according to the site of the division the organs on the affected side may either open independently into the bladder, or into a common ureter.

Ectopic Kidneys

In renal ectopia the kidney may fail to ascend, ascend to a more cranial position than is normal, or deviate to one or other side. High ectopic kidneys may be associated with congenital defects in the diaphragm, or may be accompanied by eventration of the diaphragm (Spillane & Prather, 1952; Barloon & Goodwin, 1957). Renal ectopia associated with failure of normal renal ascent was reviewed by Thompson & Pace (1937) who found that in ninety-seven cases the incidence of pelvic : iliac : abdominal organs was approximately 8 : 1 : 4. Some pelvic kidneys were fused.

Fused Kidneys

By virtue of their size and association with other structures, fused kidneys are usually prevented from ascending to their normal position and are, therefore, also ectopic. Two main varieties, horseshoe and cake kidneys, are recognized. The horseshoe variety is by far the commoner and requires no detailed description. The term 'cake kidney' is used to describe a rounded flattened pelvic mass of renal tissue which has a lobulated anterior surface and a smooth concave posterior surface; the ureters emerge from the anterior aspect of the structure. Shiller & Wiswell (1957) reported a case of cake kidney which they considered to be the tenth in the literature and another was reported by Glenn (1958). By contrast horseshoe kidneys are not infrequently observed in the dissecting or post-mortem room. The condition results from a fusion of the developing metanephric *anlagen*. According to Lewis & Papez (1915) and Boyden (1931) fusion of the developing metanephric elements results from their medial displacement during ascent; the displacement in turn being the result of an abnormal medial deviation of the umbilical arteries. Fused kidneys are usually prevented from ascending by the inferior mesenteric artery and in consequence the renal vessels arise from the lower end of the aorta or iliac vessels and represent persisting caudal mesonephric arteries or caudal parts of the rete urogenitale.