# THE DEVELOPMENT OF THE BLOOD VESSELS OF THE METANEPHROS

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## INTRODUCTION

Bowman (1842) clearly established the fundamental principle relating to the adult renal circulation, that 'all the blood of the renal artery (with the exception of a small quantity distributed to the capsule, surrounding fat, and the coats of the larger vessels) enters the capillary tufts of the Malpighian bodies; thence it passes into the capillary plexus surrounding the uriniferous tubules and it finally leaves the organ through the branches of the renal vein'. This view was later modified by the belief that the arteriolae rectae of the medulla arose directly from the arcuate branches of the renal artery without the interposition of a glomerulus (the so-called arteriolae rectae verae). Huber (1907) demonstrated the accuracy of Bowman's original concept, showing that the arteriolae rectae of the medulla were branches of the efferent arterioles of juxta-medullary glomeruli (the so-called arteriolae rectae spuriae), though degeneration of an occasional glomerulus, and its replacement by a single enlarged channel, might rarely give rise to an arteriola recta vera. This view has been confirmed and elaborated by the detailed work of Morison (1926), Moore (1928), MacCallum (1926) and Trueta, Barclay, Daniel, Franklin and Prichard (1947). Some of these authors, however, believed that there were a few branches of the interlobular arteries which did not terminate in glomeruli but ended directly in the peritubular plexus, capsule, or even perirenal tissues, but all considered these were insignificant. Huber pointed out that the vessels supplying the medulla would contain blood of increased osmotic pressure, having lost glomerular filtrate, and this would favour reabsorption of water from the loops of Henle. Moore (1928) and Traut (1923) showed that there were no anastomoses, other than those at capillary level, between branches of the renal artery, the arcuate arteries being continuations of interlobar arteries along the cortico-medullary junction but never meeting to form vascular arcades.

Felix (1912) gave the classical account of kidney development. He described the development of mesodermal metanephrogenic vesicles into S-shaped tubules whose lower limbs became double-walled cup-like structures (early Bowman's capsules) in whose concavity the glomerulus developed, by a process which he did not describe. Strangely, in an organ where the unique vascular architecture is at least as important to its function as the form of the nephrons, he made almost no mention of developing vessels. The only descriptions of vascular development to be found are confined to isolated facets of the problem, usually of glomerular development. Sabin's (1917) concept that, following a short period of development of vessels directly from mesoderm in the axis of the embryo, all subsequent vessel formation is by budding, has influenced investigators. Thus, Edwards (1951) described solid, freely-ending

buds arising from branches of the renal artery and growing towards and invaginating a Bowman's capsule where it divided to form the loops of the glomerulus; these, he said, reunited to form an efferent arteriole which grew out of the capsule and then again divided to form the peritubular plexus. He stated that at birth this process had only occurred in those glomeruli close to the medulla and that, at this time, no peritubular plexus was yet developed in the peripheral two-thirds of the cortex. Earlier and somewhat similar views suggesting an invagination of Bowman's capsule by capillary loops were held by Toldt (1874), Pye (1875) and Ribbert (1880). Others have disagreed with this view and considered that the glomeruli were formed in situ. Herring (1900) considered that the visceral layer of Bowman's capsule proliferated to form a mass of angioblastic tissue in which cavitation formed the lumen of the glomerulus which was then joined by an ingrowing branch of the renal artery. Hamburger (1890) held a rather similar view. These conflicting views all suggested that as soon as a circulation was established it was of the complicated adult pattern. The observation of Broman (1907), Jeidell (1911) and Davies (1950) that the metanephros at an early stage of development was vascularized by a simple capillary bed was difficult to reconcile with these views.

The purpose of this investigation was to study the development of the metanephric circulation from the earliest stages and thus gain an integrated picture of nephron and vascular development, for any understanding of renal function in the foetal or early post-natal period must depend on such knowledge.

## MATERIALS AND METHODS

A series of rabbit kidneys was used initially to establish the sequence of developmental changes. The kidneys of many foetal rabbits of 16–27 days gestation, injected via the umbilical artery with a colloidal dye, Monastral Fast Blue B.N.V.S. Paste (supplied by I.C.I. Ltd.) or in some cases indian ink, and also the kidneys of new born, 12 day postnatal, and adult rabbits injected via the renal artery, were used. The kidneys of 55 mm. and 90 mm. guinea-pig embryos and a 22 cm. sheep embryo were later examined.

Initially serial 100$\mu$ sections were cut on a freezing microtome after embedding the kidney in gelatin. After removing the gelatin in warm water the sections were dehydrated, cleared in methyl benzoate, and mounted.

Histological sections of 5 or 8$\mu$, stained with haematoxylin and eosin or Heidenhain's iron haematoxylin were also prepared at all stages.

A number of injected kidneys were also embedded in celloidin and serially sectioned at 100$\mu$, the sections being cleared and mounted; some sections from these specimens were cut at 20 or 40$\mu$ and stained with haematoxylin and eosin, a method which gave a good integrated picture of the developing vessels and parenchyma.

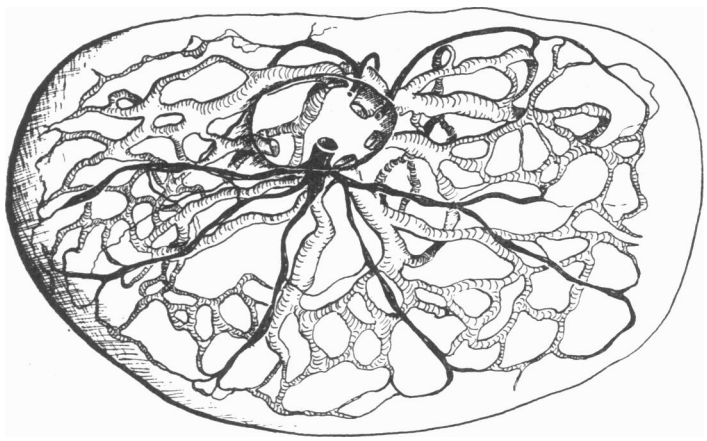
Some features of the vascular pattern were difficult to interpret from sections. It was found that, after maceration in 50% hydrochloric acid, injected kidneys could be readily dissected under the binocular microscope and a clear picture of the vascular architecture gained. This procedure was employed for kidneys of various ages.

## DESCRIPTION OF DEVELOPMENT

### *Stage* 1. *Initial vascularization of metanephrogenic tissue*

This stage is well illustrated by the kidney of a 16-day rabbit embryo. The kidney, as seen in histological sections, consists of two definite zones, an outer, darker cortex bounding a core of loose mesenchyme, the medulla, containing the ureteric outgrowth and its main branches. The outermost part of the cortex consists of proliferative, metanephrogenic tissue which is giving rise to vesicles related to the terminations of the collecting tubules situated in the cortex, and also to a small amount of loose intervening mesenchyme continuous with that of the medulla (Pl. 1, fig. 1.).

An injected preparation at this stage (Text-fig. 1) shows five or six branches of the renal vein entering at the hilum and coursing laterally over the surface of the globular medullary mass to break up into a plexus of wide-bored channels. Accompanying each vein is a much narrower and more heavily injected artery which also



Text-fig. 1. A camera-lucida drawing of the cleared kidney of a 16-day injected rabbit embryo. The peripheral cortical plexus is shown, supplied by radially running arteries (black) entering at hilum and drained by radially running, wide-bored veins (light).

breaks into branches joining the plexus. These arteries and veins run a course similar to the main branches of renal artery and vein in the adult rabbit, which course over the surface of the medulla to reach the junction of cortex and medulla, and correspond to the interlobar arteries of the human multilobar kidney.

Some of the metanephrogenic vesicles have already become S-shaped tubules and in the concavity of the lower limb, the double-walled, cup-like rudimentary Bowman's capsule, the first signs of a glomerulus are appearing. It takes the form of a strand or small mass of cells continuous at the margins of the cup with the surrounding mesenchyme. There appears to be little doubt that these cells are extruded from the thick, proliferative, visceral epithelial layer of Bowman's capsule (Pl. 1, fig. 2.).

*Stage* 2. *Vascularization of the developing cortex and medulla*

21-*day rabbit embryo*

The cortex is thickened and contains many developing nephrons and the loose mesenchymal medulla now contains, in addition to the main branches of the collecting ducts, loops of Henle, protruded into it from the cortex. The loose tissue of the medulla is continuous with the mesenchyme between the tubules of the cortex and this merges imperceptibly into the outermost neogenic zone of the cortex where it is presumably arising.

Injected specimens at this stage (Pl. 1, fig. 3) show a cortex occupied by a dense plexus of vessels and arising from this plexus are straight parallel channels, the vasa recta, passing into the medulla and anastomosing or looping back in the deepest part of the medulla. The cortical plexus fulfils the criteria of Minot (1898, 1900) for a sinusoidal system and gives, as it were, a negative picture of the tubular pattern. The vascular channels are angular, their walls follow the shape of the parenchyma of the organ, they are of larger size than capillaries and are freely and widely communicating; capillaries, on the other hand, are narrow and their walls follow their own curve. The intimate relations between vessel and tubular wall are clearly seen in stained injected sections (Pl. 1, fig. 4; Text-fig. 2); in many places it is difficult to distinguish any wall to the vessel though an occasional flattened nucleus is seen. Uninjected haematoxylin and eosin sections at this stage show mesenchymal strands between the tubules merging imperceptibly into the outer neogenic zone on the one hand and continuous with the mesenchyme of the medulla on the other. The cortical sinusoids are with little doubt developing as spaces in these mesenchymal strands; as the cavitation with formation of lumina proceeds the mesenchyme is pressed against the tubules to form the sinusoid walls which are presumably complete. As more metanephrogenic vesicles and intervening mesenchyme are produced peripherally from the neogenic zone, extension of lumen formation in the mesenchyme extends the plexus centrifugally. Thus, in stained injected specimens the dye-filled lumina are frequently seen extending up to the neogenic zone and tailing off blindly into the dense cellular mass composing it. The vasa recta in the medulla either arise similarly or perhaps by budding from the cortical plexus.

Glomerular development is much advanced on the previous stage and several generations of glomeruli are present, the oldest being closest to the medulla. The youngest have a similar form to those seen at the 16-day stage, the glomerular anlage being formed apparently from the visceral layers of Bowman's capsule. A little deeper (and older) the glomerular anlagen consist of solid masses of cells continuous with the surrounding mesenchyme in which the sinusoids are forming. The visceral layer of Bowman's capsule is still tall and seems to be making a contribution to it (Pl. 1, fig. 5). Many of the deepest glomerular anlagen are loosening in texture and commencing to form a spongework of spaces, especially peripherally, in which a few red blood corpuscles may be seen; the visceral capsular epithelium has thinned and the glomeruli are showing commencing lobulation (Pl. 1, fig. 6). Rarely in stained injected sections dye is found in the spaces of such a glomerulus (Pl. 1, fig. 7) and very occasionally the dye-filled lumen of an adjacent sinusoid extends into the mesenchymal strand of one of the earliest glomeruli. The process of glomerular

development can now clearly be seen. Strands of mesenchyme between the tubules are produced from the neogenic zone and are continuous with other similar but closely packed cellular masses in the concavity of the cup-like Bowman's capsules and presumably derived from their visceral layer, and thus having a similar mesodermal origin. The sinusoidal plexus develops in the intertubular region and the glomerular anlagen are closely related to the sinusoids which closely invest the developing Malpighian bodies. Cavities appear in the pre-glomerular mass and even at this stage some of the older glomeruli have these developing lumina linked with the sinusoids as shown by the presence of injection mass or red blood corpuscles. A similar canalization of the earliest glomerular strands may be seen for a short time, but they soon become dense and solid. The circulation at this stage is through the sinusoids and any circulation through the glomeruli is minimal and in the nature of a sluggish side channel.

To understand the arterial supply and venous drainage of the cortical sinusoids, which in turn supply the vasa recta of the medulla, the topography of a unilobar kidney must first be appreciated; the arteries and veins corresponding to the interlobar vessels of the multilobar kidney pass in grooves over the dorsal and ventral surfaces of the medulla and the medulla approaches and merges into the cortex between them—the appearance is that of a multilobar kidney with the apices of the medullary pyramids fused. Sections near the dorsal and ventral surface give an appearance similar to a multilobar kidney. Cleared sections of injected preparations at this stage show large veins in this position continuous with the cortical sinusoidal network, but no arterial supply is apparent (Pl. 1, fig. 8). The possibility of a purely venous portal circulation at this stage was considered, as Broman (1907) has suggested. However, arteries are seen to be present at the 16-day stage and Jeidell (1911) has also observed an arterial supply from very early stages, and, moreover, definite arteries can be seen in stained injected preparations, but without dye in their lumina (Pl. 1, fig. 4.). Dissections of injected specimens show very thick-walled dye-filled branches of the renal artery, entering at the hilum, but the dye tails off as the artery is traced towards the cortex, though the empty arterial branches can still be followed into continuity with the sinusoids. These arteries are obviously pouring blood into the sinusoids which, being very capacious and of low resistance, do not provide sufficient back pressure to maintain filling of the arteries.

*23-day rabbit embryo*

Injected preparations show a similar pattern to the 21-day stage with a rather thicker cortex whose vessels are more capilliform, having their own form rather more than the form of the parenchyma. No injected glomeruli are yet seen (Pl. 1, fig. 9).

Histological sections show only slight advance on the 21-day stage, all stages of glomerular development being present, but even the oldest and deepest glomeruli are still fairly dense in structure, though some red blood corpuscles are seen in their spaces.

Stained injected sections show no dye in the glomeruli and the circulation is obviously predominantly through the sinusoids, little traversing the glomeruli. The arterial supply is similar to the 21-day stage.

*24-day rabbit embryo*

Injected preparations show a similar picture to the previous stage. In injected stained preparations a few glomeruli of all stages, even the earliest (Pl. 1, fig. 10), are showing ink in their spaces, and many, especially the older ones, are loosening their texture considerably and contain many blood cells. Obviously vascularization of the glomeruli is advancing.

*25-day rabbit embryo*

The only specimen to be described at this stage is an incomplete injection. A characteristic pattern is obtained with only the regions of the cortex between the medullary rays being injected, no injected glomeruli being seen and no, or few, vessels being present in the medullary rays. The arteries are well injected and their continuity with the cortical plexus is clearly established (Pl. 1, fig. 11). The cortical plexus retains much of its sinusoidal character, and it is probable that more complete injection would have filled some glomeruli. The vascular regions injected represent the adjacent cortical surfaces of two lobules, establishing the fact that there is, at this stage, continuity between the capillary beds of adjacent lobules. Traut (1923) maintains that there is little anastomosis in the adult between the capillary beds of adjacent lobules. It is apparent that, since the arteries drain into the wide-bored cortical capillary bed, of which the glomeruli are side channels of high resistance, an incomplete injection would produce the picture seen here of discontinuous injected interlobular regions in the cortex.

*Stage 3. Vascularization of glomeruli*

*26-day rabbit embryo*

Histological sections at this stage show glomeruli at all stages of development, including the earliest, while the oldest generation have become very spongy, the spaces often containing red cells, and the visceral epithelium of Bowman's capsule being flattened.

Glomeruli are now seen in injected preparations, the youngest being small balls of two or three tortuous channels, while the oldest are large and complicated. Narrow-bored, heavily-injected arteries pursuing a definite course through the cortical plexus are seen; they give off afferent arterioles to the glomeruli but also become continuous, by gradual transition, with the plexus (Pl. 2, fig. 12). The glomeruli are obviously establishing continuity of their spaces with the surrounding sinusoids, which are now capilliform. From the point of entry of the original arteries definite arterial channels are developing from the component vessels of the plexus towards these glomeruli—these arteries become the interlobular branches of the arcuate arteries; they retain their connexion, especially peripherally, with the plexus from which they are derived. It has been seen that the vasa recta arise in continuity with the cortical plexus, but by this stage definite channels are forming from the plexus towards the juxta-medullary glomeruli, to produce the vasa recta spuriae, though this process is not yet complete. Incompletely injected parts of the kidney at this stage show the radial interlobular pattern in the cortex (Pl. 2, fig. 12) noted in the 25-day stage and these areas show few injected glomeruli. It would seem that

the direct connexions of the arteries with the plexus show less resistance to the flow of blood (or dye) than the glomeruli. In some situations the cortical plexus has established continuity with the capsular vessels and here the cortex is more heavily injected.

Dissected specimens at this stage (Pl. 2, fig. 13) show with great clarity the connexions of the arteries with glomeruli and also the retention of their more primitive, wide, direct connexions with the cortical plexus in the outer half of the cortex. They also show how the vasa recta are developing connexions only with the juxta-medullary glomeruli, from the plexus.

*27-day rabbit embryo*

Injected preparations are similar to the previous stage, with the cortical plexus now having a fairly definite capillary form and with glomeruli of all stages of development present. Some specimens, in which injection was incomplete show the pattern, already noted, of injection of the peritubular plexus in interlobular regions, without injection of glomeruli. The vasa recta retain many connexions with the cortical plexus (Pl. 2, fig. 14), from which they receive most of their blood, though the development of definite thin, discrete channels from the plexus connecting them with juxta-medullary glomeruli is continuing. Direct continuity of arteries with the peritubular plexus is still seen. Stained injected preparations show various stages of development and vascularization of glomeruli (Pl. 2, fig. 15).

*New-born rabbit*

Development has progressed but the pattern is fundamentally the same as the previous and the arteries retain direct communications with the peritubular plexus. Histological sections show that there is still a neogenic zone and Malpighian bodies are still being formed.

*12-day old rabbit*

One specimen at this stage was fully injected in some areas and here showed many glomeruli, but much of it was incompletely injected and showed the typical interlobular injection without glomeruli (Pl. 2, fig. 16), already noted at other stages and due to continuity between arteries and peritubular plexus. In the more fully injected regions the continuity of arteries both with glomeruli and with the cortical plexus, which is now clearly of capillary nature, can be clearly seen (Pl. 2, fig. 17) and this is also well shown in dissections of injected preparations. The development of definite connexions between vasa recta and juxta-medullary glomeruli is continuing but by no means yet complete.

Histological sections show some very early glomeruli but the neogenic zone is virtually exhausted and new formation of nephrons and glomeruli is just ceasing.

*15-day rabbit*

New formation of glomeruli has ceased, the neogenic zone is exhausted, and a cortex corticis, an outer zone of cortex consisting of tubules only and no glomeruli, is formed.

*55 mm. guinea-pig embryo*

This is a typical specimen of the stage of vascularization of glomeruli and shows connexions of interlobular arteries with both glomeruli and peritubular plexus.

*90 mm. guinea-pig embryo*

This specimen is well injected in only a small segment of the kidney and shows here injected glomeruli and also the continuity of the interlobular arteries with the plexus in the outer part of the cortex (Pl. 2, fig. 18). The remainder of the kidney is poorly injected and here shows the typical interlobular pattern (Pl. 2, fig. 19), without glomeruli, due to injection of the plexus through its direct communications with the interlobular arteries.

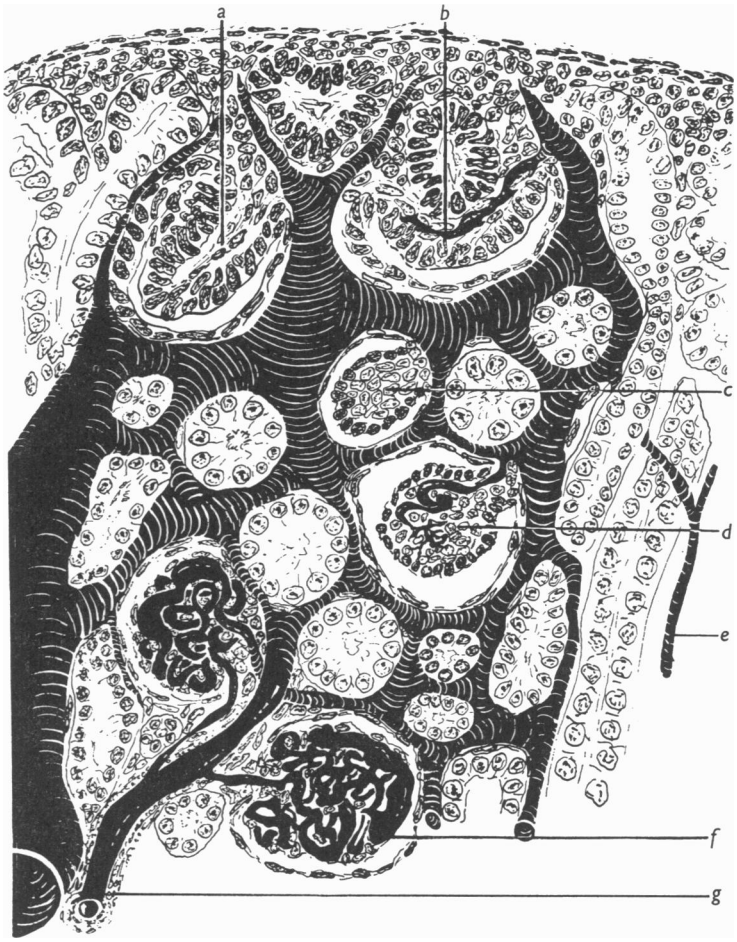
*22 cm. sheep embryo*

This is also at the stage of developing vascularization of glomeruli, and shows the afferent arterioles of injected glomeruli arising from the interlobular arteries and the continuity of these arteries with the peritubular plexus in the outer half of the cortex (Pl. 2, fig. 20).

## DISCUSSION

It is apparent that the blood vessels of the kidney, after the initial ingrowth of branches of the renal artery and vein, arise *in situ*. The outermost neogenic zone, besides giving rise to metanephrogenic vesicles, also forms intertubular mesenchyme and the glomerular anlagen, almost certainly, arise by proliferation from the visceral layer of Bowman's capsule and are continuous with the intertubular mesenchyme. Cavitation with lumen formation in the intertubular mesenchyme gives rise to the cortical vessels, which have a typical sinusoidal form and this lumen formation may extend into the earliest glomerular strands as shown by the presence of red blood corpuscles or injection mass. Increased proliferation, however, soon makes the glomeruli very dense and circulation in them must then be minimal. As the glomeruli become more mature they loosen in texture and their spaces link up with the surrounding sinusoidal lumina, and following this, changes occur in the cortical plexus (Text-fig. 2). Definite arterial channels develop through the plexus from the points where the branches of the renal artery join it, this process probably being dependent on increased flow through certain of the channels of the plexus coincident with the opening up of the glomeruli. The principles of Thoma (1896), may govern this process. The first principle states that a channel in a plexus increases in size if the rate of blood flow in it increases and conversely those vessels in which blood flow stops disappear; the second principle states that a vessel wall grows in thickness when its tension increases. However, as Hughes (1943) has suggested, factors other than purely functional ones may determine the development of arteries and veins from a vascular plexus. However, whatever the mechanism, the cortical plexus is remodelled to produce arterial channels leading to the glomeruli, but these arteries, during the period of development, remain continuous by wide communications with the plexus in the outer and primitive part of the cortex. Indeed these direct communications would seem to offer least resistance to the blood flow, for incomplete

injections tend to fill the cortical plexus through them without injecting the glomeruli. These direct communications between interlobular arteries and peritubular capillaries, which constitute a shunt by-passing the glomeruli, persist into postnatal life, e.g. at least 12 days in the rabbit. The vasa recta of the medulla initially




**Text-fig. 2. A diagram of the thickness of the cortex of a developing injected kidney, showing the manner in which the glomeruli are vascularized. (*a*) A very early glomerulus, not vascularized. (*b*) A similar glomerulus containing a strand of dye continuous with surrounding sinusoids. (*c*) A medium-age glomerulus, dense and unvascularized. (*d*) Commencing vascularization of a glomerulus. (*e*) Vasa recta entering medullary ray from sinusoidal plexus. (*f*) Well-vascularized glomerulus. (*g*) Artery elaborating from the cortical plexus and lying beside a large vein draining the plexus.**

are continuations of the cortical plexus, before the glomeruli are vascularized, arising either *in situ* in the medulla or by budding from the cortical plexus. A remodelling of the deepest part of the cortical plexus produces their definitive origin from the juxtamedullary glomeruli but even into postnatal life (in the rabbit at least) much blood must enter them directly from the peritubular plexus, which

is receiving blood, in part, directly from the arteries. Hence, the blood in the vasa recta at this stage is not of increased osmotic pressure as it is in the adult.

It has been seen that the sinusoids of the cortex arise *in situ*. Minot (1900) has written that sinusoids arise by a mutual intercrescence of the parenchyma of an organ and the endothelium of a vein, but Streeter (1942) has shown that in the liver they arise, at least in part, *in situ*. It would seem probable from their form, with lining cells pressed closely against the parenchyma, that sinusoids in general arise *in situ* by a confluence of mesenchymal spaces which press the mesodermal cells against the parenchyma, forming their endothelial walls. Minot (1898) has considered that the cortical capillaries of the adult kidney signified a morphological difference between the metanephros on the one hand and the mesonephros and pronephros on the other; here we have seen that cortical sinusoids do exist in the foetal metanephros, thus establishing its close relationship to the mesonephros and pronephros. The description here of glomerular development in the metanephros is similar to that of Herring (1900) and is in close agreement with that given for the development of mesonephric glomeruli by Streeter (1945), J. Davies & D. V. Davies (1950) and J. Davies (1950). There is a striking similarity between this glomerular development and that of the spleen (Lewis, 1956)—in both a thick proliferative mesodermal epithelial surface gives rise to a dense mass of cellular angiogenic tissue in which spaces appear giving rise in the spleen to the various components of its vascular system and to the capillaries of the glomerulus in the kidney. Thus, the development *in situ* of cortical sinusoids and glomerular capillaries are exceptions to Sabin's concept of vascular development by budding and no evidence was found for Edwards's (1951) view of the development of the glomeruli and remainder of the kidney vasculature from ingrowing vascular sprouts.

This knowledge of the blood supply of the developing kidney throws light on many of the results of investigations of kidney function in the foetal and early postnatal period. Gersh (1937), using an experimental method has found that glomerular filtration commences after about 21 days gestation in the foetal rabbit but he considers that urine formation is remarkably slow in the foetus. McCance & Widdowson (1956, 1957) have noted the low glomerular filtration rate just after birth, using surface area as a basis of comparison, and Feldman (1920) has described a rapid increase in the daily amount of urine produced during the first 6 days of postnatal life in the human, and thereafter a slower increase. McCance and Widdowson also find that the urea clearance, related to surface area, is lower in the first 14 days of life than in the adult and they find that the blood urea rises after birth for 48–72 hr. in piglets and the human, due to 'immaturity of renal function'. The blood urea is the result of a balance between breakdown of protein and its elimination in the kidney and any increase in tissue breakdown of protein (e.g. after difficult labour) may give rise to high serum urea levels. They consider that in slow-growing animals (e.g. man) where the renal elimination is more important than growth in maintaining a reasonable level of blood urea, the kidney is more highly developed at birth than in fast-growing animals (e.g. pig, rat). Gersh considers that a low glomerular capillary pressure might be responsible for slow urine formation for it is known (Clark, 1932) that the blood pressure in the foetus is low and the adult level is not reached until some weeks or even years after birth, depending on the species.

However, in such functions as glomerular filtration this tends to be balanced by a lower protein osmotic pressure (Clark and Holling, 1931). Thus, the low glomerular filtration rate and slow output of urine in the foetus and new-born could not be explained entirely on the basis of a low blood pressure if the vascular pattern was the same as that of the adult. It is also known (McCance & Widdowson, 1957; Feldman, 1920) that the urine of an early postnatal animal is less concentrated than that of the adult, and as the output increases, so does the specific gravity.

Edwards (1951) has attempted to explain the physiology of the new-born kidney on the assumption that at birth only the medulla and a narrow zone of cortex bordering it have a functional blood supply, in effect the shunt as described by Trueta *et al.* However, this cannot be so, for Edwards concept of circulation in the foetal kidney has been found to be without foundation. Gruenwald and Popper (1940) describe the tall visceral layer of Bowman's capsule as persisting until after birth and maintain that it impairs filtration in the foetal kidney but although this is probably a factor it can only provide a partial explanation for even in a 21-day foetal rabbit this epithelium is flattened out in the oldest glomeruli.

In the description of development given here it has been seen that continuity of the interlobular arteries with the peritubular cortical plexus, persisting for a time in postnatal life, acts as a by-pass short-circuiting much of the blood of the renal artery past the glomeruli. Indeed, in incomplete injections the peritubular plexus was injected without filling of the glomeruli and it is probable that with the low blood pressure of foetal and early postnatal life much of the circulation follows this by-pass, producing a low glomerular filtration rate. It has also been seen that the vasa recta in the foetal and early postnatal period arise directly from the cortical capillary plexus, which is receiving much of its blood from the glomerular by-pass, and so will not contain concentrated blood as in the adult (Huber, 1907), which presumably will impair reabsorption of water from the loops of Henle and may account for the less concentrated urine of the new-born animal.

## SUMMARY

1. The circulation in the kidney at an early stage consists of a cortical sinusoidal plexus giving rise to vasa recta entering the medulla.

2. The glomeruli arise as angiogenic masses proliferated from the visceral layer of Bowman's capsule. Cavitation produces their lumina which link up with the sinusoids of the cortex.

3. When circulation is established in the glomeruli remodelling of the cortical plexus produces arterial branches leading up to them, but wide communications of these arteries directly with the plexus are retained in the outer less differentiated part of the cortex, even into the early postnatal period.

4. The anatomical and physiological significance of these findings is discussed.

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## EXPLANATION OF PLATES

### PLATE 1

Fig. 1. A 5 $\mu$ section of the kidney of a 16-day rabbit embryo stained with haematoxylin and eosin. $\times 45$.

Fig. 2. The same kidney as fig. 1. Part of the S-shaped developing nephron is seen, showing the middle limb (*a*), the flattened parietal layer (*c*) of the developing Bowman's capsule, and the visceral layer (*b*) apparently giving rise to the cells of the glomerular anlage. $\times 320$.

Fig. 3. A cleared 100 $\mu$ section of a monastral fast blue injected 21-day rabbit embryo kidney; the cortical sinusoidal plexus and the vasa recta of the medulla are shown. $\times 46$.

Fig. 4. A haematoxylin and eosin stained 40 $\mu$ section of a monastral fast blue injected 21-day rabbit embryo kidney. An uninjected artery is seen at (*a*). $\times 20$.

Fig. 5. A 5 $\mu$ haematoxylin and eosin section of a 21-day rabbit embryo kidney. A medium-age Malpighian body is shown and the visceral layer of Bowman's capsule appears to be still making a contribution to the compact glomerular anlage. $\times 400$.

Fig. 6. A more mature glomerulus from the same kidney as fig. 5. The glomerulus is loosening and the epithelium covering it is now flattening. $\times 400$.

Fig. 7. A haematoxylin and eosin 40 $\mu$ section of a monastral fast blue injected 21-day rabbit embryo kidney. A loosening glomerulus (*a*) is seen which contains some injection mass and the cortical sinusoids closely investing nearby tubules are seen. $\times 200$.

Fig. 8. A 100 $\mu$ cleared section of a monastral fast blue injected 21-day rabbit embryo kidney showing the large radially arranged veins draining the cortical sinusoids. $\times 33$.

Fig. 9. A 100 $\mu$ cleared section of a monastral fast blue injected 23-day rabbit embryo kidney. The cortical sinusoids are shown giving rise to the medullary vasa recta, and several of the large veins draining the sinusoids are seen. No injected glomeruli are yet seen. $\times 50$.

Fig. 10. An 8 $\mu$ H. and E. section of an indian ink injected 24-day rabbit embryo kidney. A strand of ink (*a*) is present in the glomerular anlage and some ink can be seen clinging to the walls and lining surrounding sinusoids. $\times 320$.

Fig. 11. A 100 $\mu$ cleared section of a monastral fast blue injected 25-day rabbit embryo kidney. Injection is incomplete and there is a radiate arrangement of vessels in the cortex. An artery (*a*), accompanied by a vein, is passing to join the cortical plexus. $\times 36$.

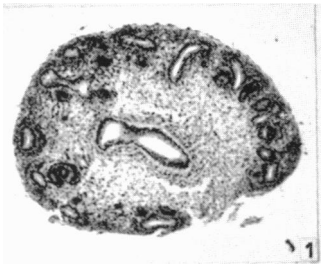
### PLATE 2

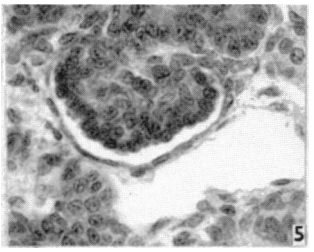
Fig. 12. A 100 $\mu$ cleared section of a monastral fast blue injected 26-day rabbit embryo kidney. An arcuate artery (*a*) lies near the cortico-medullary junction and it or its branches supply afferent arterioles to several glomeruli; several peripherally running interlobular branches are joining the cortical plexus directly. $\times 88$.

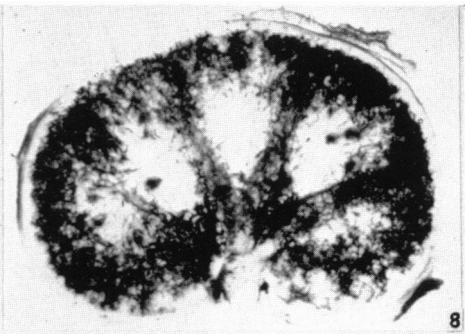
Fig. 13. A dissection of a monastral fast blue injected 26-day rabbit embryo kidney. An arcuate artery (*a*), accompanied by a large vein, gives rise to interlobular branches, from which spring the afferent arterioles of a number of glomeruli, and which draindirectly into the peritubular plexus peripherally. $\times 65$.

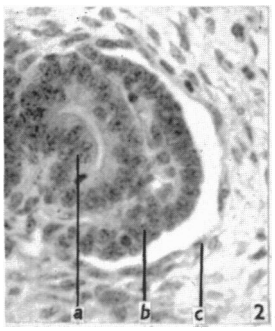
Fig. 14. A 100 $\mu$ cleared section of a monastral fast blue injected 27-day rabbit embryo kidney. Cortex containing some injected glomeruli and part of medulla containing vasa recta are shown. $\times 33$.

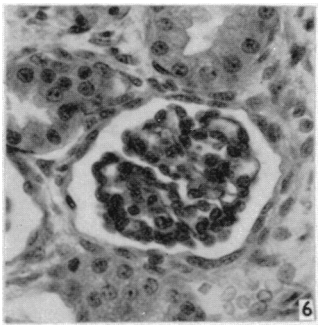
Fig. 15. A 40 $\mu$ H. and E. section of a 27-day monastral fast blue injected foetal rabbit kidney. Two glomeruli are shown in which canalization of the glomerular anlagen is proceeding and the lumina formed are filled with dye. $\times 200$.

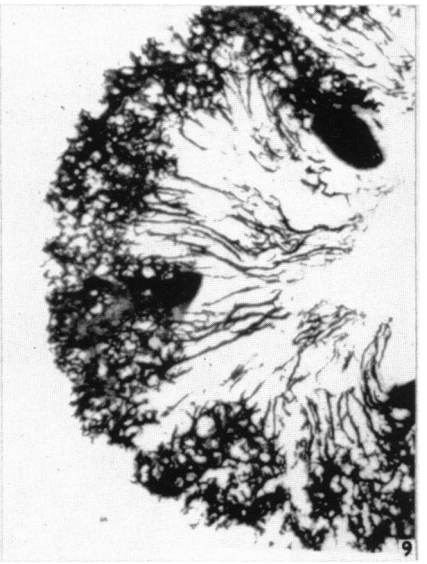


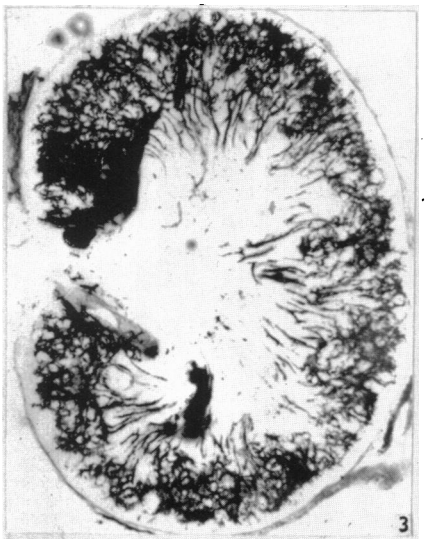



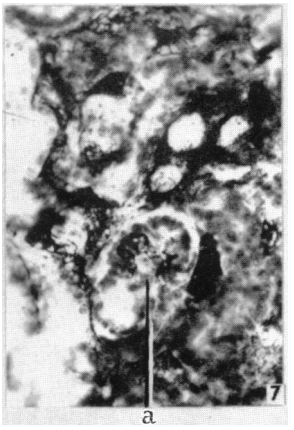



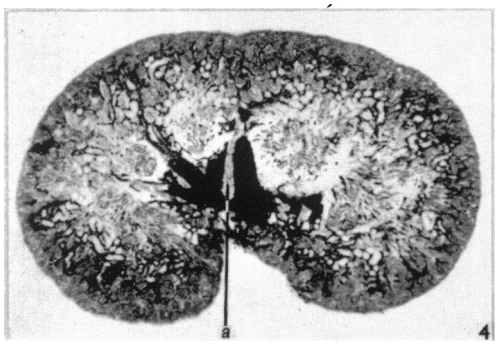



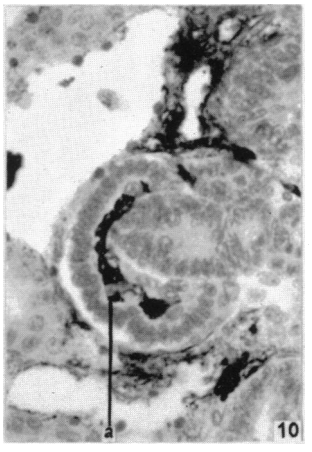



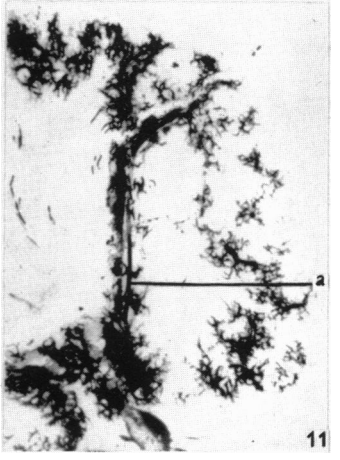




LEWIS—Development of the blood vessels of the metanephros

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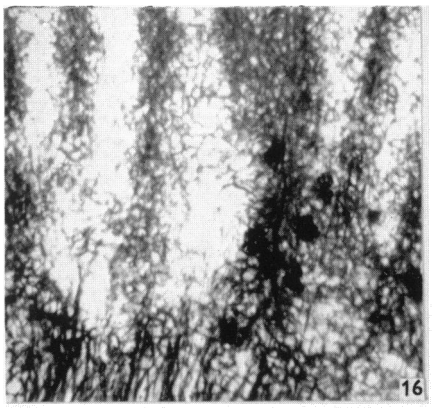
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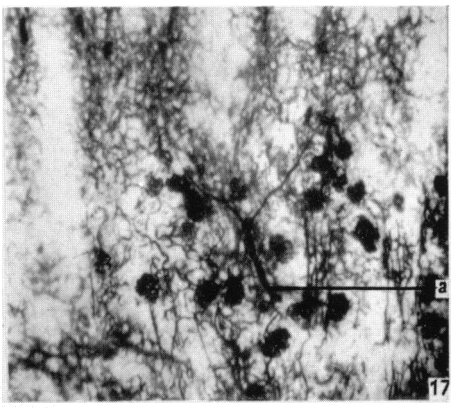
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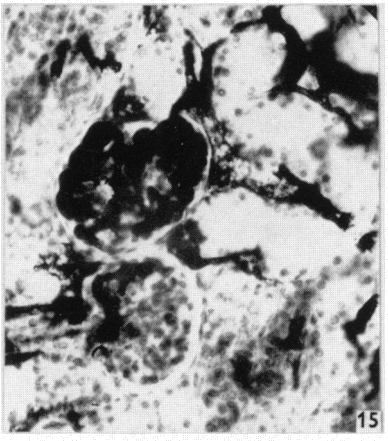
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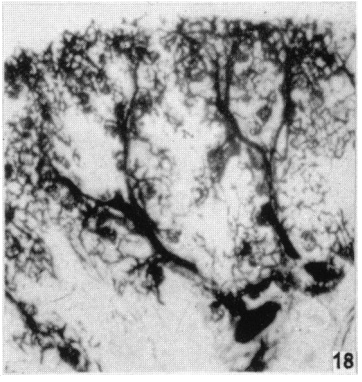
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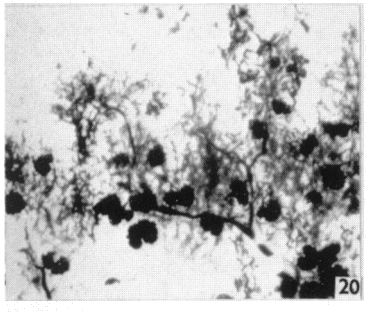
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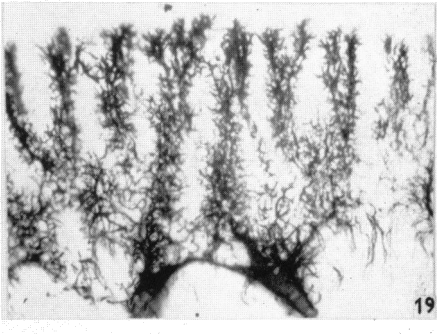
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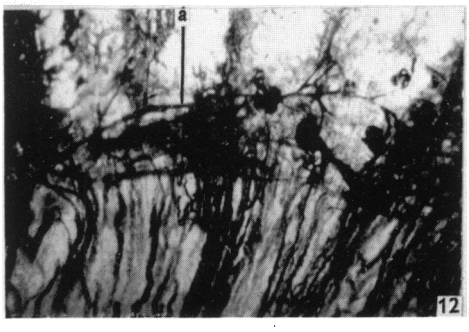
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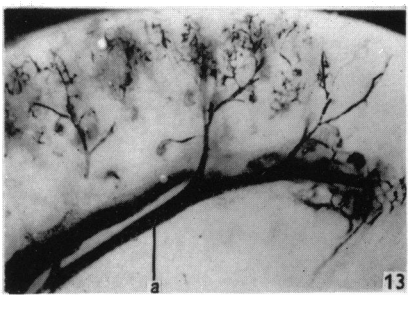
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Fig. 16. A 100 $\mu$ cleared section of a 12-day postnatal rabbit kidney injected with monastral fast blue. To the right an interlobular artery supplies glomeruli and terminates in the peritubular plexus. Injection is incomplete towards the left and glomeruli are not injected. × 110.

Fig. 17. The same kidney as fig. 16. An interlobular artery (*a*), after giving afferent arterioles to glomeruli, terminates as two branches joining the cortical plexus. × 110.

Fig. 18. A 100 $\mu$ cleared section of the kidney of a 90 mm. guinea-pig embryo injected with monastral fast blue. Interlobular arteries supply glomeruli and terminate peripherally in the peritubular plexus. × 106.

Fig. 19. A 100 $\mu$ cleared section of the kidney of a 90 mm. guinea-pig embryo injected with monastral fast blue. The region shown is incompletely injected and glomeruli are not filled but the cortical plexus is seen together with a vein draining it. × 64.

Fig. 20. A 100 $\mu$ cleared section of the kidney of a 22 cm. sheep embryo injected with monastral fast blue. An artery is shown dividing, supplying glomeruli, and terminating in the peritubular plexus. × 110.