Lecture Notes on Nephrology

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Preface

In the past few years there has been a proliferation of short textbooks in various specialities including nephrology, so that students are spoilt for choice. How then does one choose the right book? As medical curricula expand, students are expected to assimilate more and more facts. Therefore, condensation of what is important without dressing it up to appear complicated would seem to us to be of prime importance. This is what we have tried to do in this edition of *Lecture Notes on Nephrology*. This is not intended to be a comprehensive textbook but a list of suggested Further Reading is included to satisfy those inclined to more profound enquiry.

We would like to acknowledge the help and encouragement given by our wives during the lengthy gestation of this book, the expert secretarial help from Mrs J. Small who typed the countless proofs and the patience of Mr Peter Saugman of Blackwell Scientific Publications.

Finally, we are grateful for the help and forebearance of our past teachers, colleagues, nursing colleagues and patients, without which we would not have been able even to attempt to write this book.

D.B. Evans
R.G. Henderson

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Chapter 1
History Taking and Examination in Renal Disease

INTRODUCTION

Occasionally a patient may give a brief history which by its very nature will lead to a rapid diagnosis. A sore throat followed two weeks later by oliguria may well lead to the correct diagnosis of acute glomerulonephritis, whilst a history of colicky loin pain extending to the testicle followed later by the passage of a stone in the urine leaves no doubt as to the diagnosis. Similarly, examination may provide all the clues necessary to make a diagnosis but in general this is unusual. More often the patient will have suffered a chronic illness extending over many years sometimes from childhood so that aetiological clues will have to be carefully sought. The presence of significant renal disease not yet severe enough to cause symptoms may well be missed unless the urine is tested. This simple investigation should *always* be performed as part of the physical examination and failure to do so is a serious error.

Diagnostic features of the history and examination will be found in the relevant sections of this book but a few points are worth emphasizing.

HISTORY

1 Since many disease processes affecting the kidneys are chronic the past and present medical histories often merge.

2 In early childhood, persistent enuresis, intermittent fevers, dysuria, loin or abdominal pain, vomiting and episodes of non-specific ill-health may all point towards recurrent urinary infections which may lead to scarring and impairment of kidney growth.

3 Pregnancy is a good test of renal function and enquiry should be made whether pregnancies were complicated by urinary infection, hypertension, or ankle swelling.

4 Medical examinations performed for insurance purposes or on

entry or discharge from the services may also provide a clue as to the presence of hypertension or proteinuria.

5 A past history of acute glomerulonephritis may be elicited. The patient may recall an illness characterized by swelling of the face and ankles which led to a long period of absence from school and considerable bed rest.

6 A history of loin pain is important:

(a) where it occurs during micturition spreading from the suprapubic region up to one or other of the loins, which would suggest reflux nephropathy;

(b) starting in the loin area and radiating down to the testicle and associated with haematuria and perhaps grit or gravel in the urine when a diagnosis of renal calculus is likely;

(c) a non-specific loin pain particularly occurring at periods of high fluid intake and associated with a normal urinary sediment might suggest the diagnosis of hydronephrosis;

(d) progressively worse loin pain associated with malaise and weight loss may indicate a renal tumour.

7 Abnormal bladder function should be sought since this may predispose to infection, calculus formation and reflux. Enquiries should be made about initiation of micturition, strength of stream and terminal dribbling. The capacity to pass a significant amount of urine a few minutes after micturition would suggest either ureteric reflux, a bladder diverticulum or incomplete emptying of the bladder.

8 Proteinuria may be suggested by frothy urine and if this is severe enough to cause hypoalbuminaemia then ankle oedema may occur.

9 Renal involvement leads to a loss of concentrating ability early on and this will manifest itself as nocturnal frequency.

10 Enquiry should be made into all systems since renal involvement may be part of a multisystem disease such as diabetes mellitus, multiple myeloma, amyloidosis or tuberculosis.

11 The family history is important. Where there is a history of renal failure then the possibility of polycystic disease, Alport's syndrome etc. should be considered. A knowledge of genetics will provide additional information, for when renal disease is associated with deafness, Alport's syndrome is very likely, whereas a family history of renal calculi might suggest renal tubular acidosis, cystinosis, oxaluria, etc.

12 A drug history is nowadays most important. Certain agents are directly nephrotoxic, e.g. cephaloridine, gentamicin, while others

may, in certain individuals, cause an acute interstitial nephropathy, e.g. antipyretics and thiazide diuretics. It is particularly important where acute renal failure has developed in hospital to find out what drugs the patient has received for they may be responsible for the problems. Analgesic abuse should be sought in every patient presenting with chronic renal failure. It is often useless to ask the patient directly whether he has been taking analgesics since this may lead to a denial but rather, the patient should be asked whether he has suffered from any chronic pain and whether he has bought medication from the chemist for this. The length of time that a hundred tablets would last the patient usually gives a reasonable guide to ingestion.

13 Occupational history is important, for exposure to substances such as lead, dry cleaning fluids, etc., can lead to renal damage. There is increasing evidence that exposure to hydrocarbons in all sorts of occupations may be associated with an increased incidence of glomerulonephritis.

EXAMINATION

In terms of physical signs renal disease is rather disappointing compared with diseases affecting the chest or cardiovascular systems. However, the following are important.

1 Occasionally the patient will have all the clinical signs of one of the syndromes such as chronic renal failure (see p. 125) or the nephrotic syndrome (see p. 74).

2 The kidneys should be palpated, for if one or both are palpable, a diagnosis of polycystic disease, hydronephrosis, tumour, etc., is likely.

3 The presence of an enlarged bladder would suggest lower urinary obstruction. If of long standing, this is likely to lead to infection, stone formation and renal impairment.

4 Pyrexia in the presence of tenderness over the bladder or the kidneys suggests infection and perhaps abscess formation.

5 The blood pressure should always be measured both lying and standing and an assessment should be made of the patient's fluid status. If the blood pressure is raised, then its effect upon target organs particularly the fundi and heart, should be sought.

6 Finally, evidence of multisystem disease should be looked for.

URINE EXAMINATION

This is mandatory in all patients whatever their complaint. Stick testing will reveal the presence of protein, blood and glucose in a semi-quantitative manner. Additional information may be gleaned by urine microscopy but, unfortunately, this has now been relegated to the laboratory from the ward side rooms. Some reagent sticks contain nitrite-detecting reagents which, in the presence of certain bacteria, convert the nitrate derived from metabolites into nitrite thereby suggesting urinary infection. Unfortunately this test lacks sensitivity and its use may lead to urinary infections being missed. Whenever a suspicion of urinary pathology is raised a urine sample should be submitted to the laboratory for microscopy and culture.

Chapter 2
Anatomy

The kidneys are paired organs situated high in the retroperitoneal regions of the abdomen and in relation to the 10th, 11th and 12th ribs. The right kidney lies slightly lower than the left (Fig. 2.1). Each measures approximately 12–14 cms in length when fully grown and weighs about 150 g (Fig. 2.1). Normally the blood supply via the renal arteries comes direct from the aorta and the renal veins drain into the inferior vena cava. Urine collects in the renal pelvis which leads via the ureters to the bladder.

The surface of each kidney is smooth and is a purplish-brown colour. It has a thin capsule.

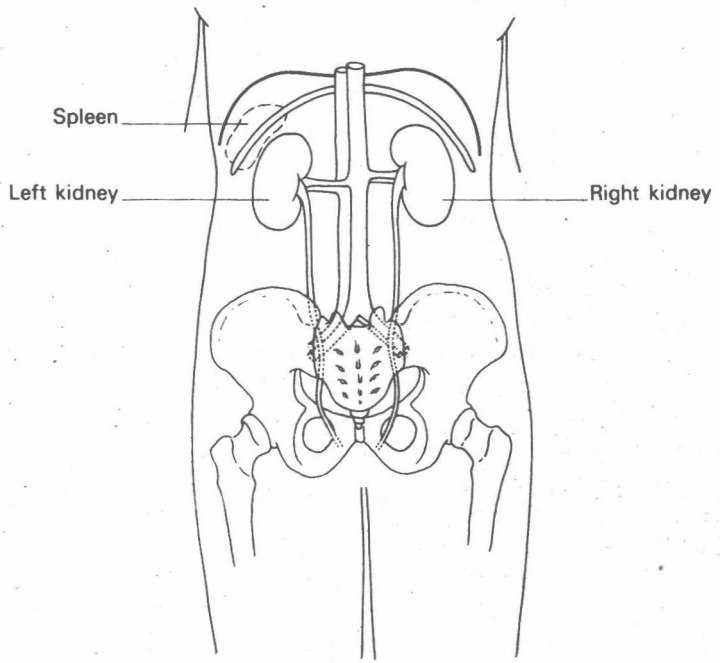

Fig. 2.1 The anatomical position of the kidneys (posterior view).

The cut surface of the kidney shows clearly defined structures—a cortex and medulla, pyramids, calyces and pelvis. Between each pyramid lie the columns of Bertini.

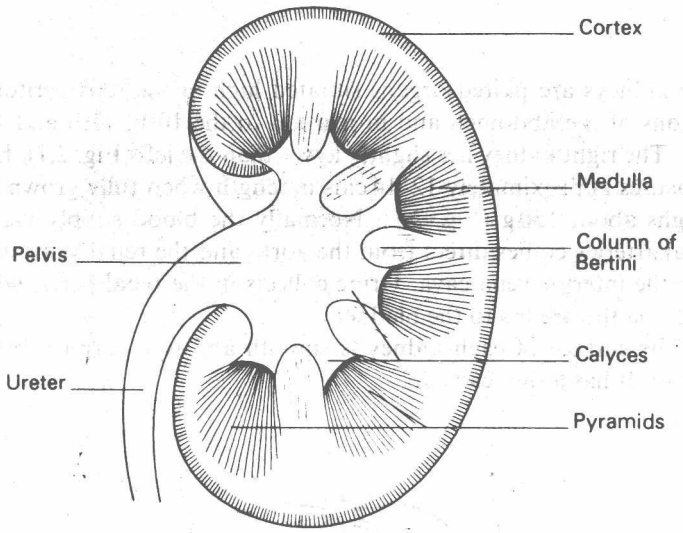

Fig. 2.2 A section through the normal kidney.

BLOOD SUPPLY

The kidney may be supplied by a single artery or by multiple arteries. These, in turn, may branch before entering the hilar structures. Inside the kidney they divide to form interlobar arteries which traverse the renal medulla as far as the corticomedullary junction. Arcuate arteries are then formed from the interlobar arteries and these run parallel to the outer surface of the kidney and at right angles to the interlobars at the corticomedullary junction (Fig. 2.3). From the arcuate arteries rise the interlobular arteries which pass into the cortex and from which the afferent glomerular arterioles arise. From the efferent glomerular arterioles emerges the bed of peritubular capillaries which either empties into peritubular venules or plunges alongside the loops of Henle into the medulla to form the vasa recta. They eventually drain into the venous system which follows anatomically the arterial system.

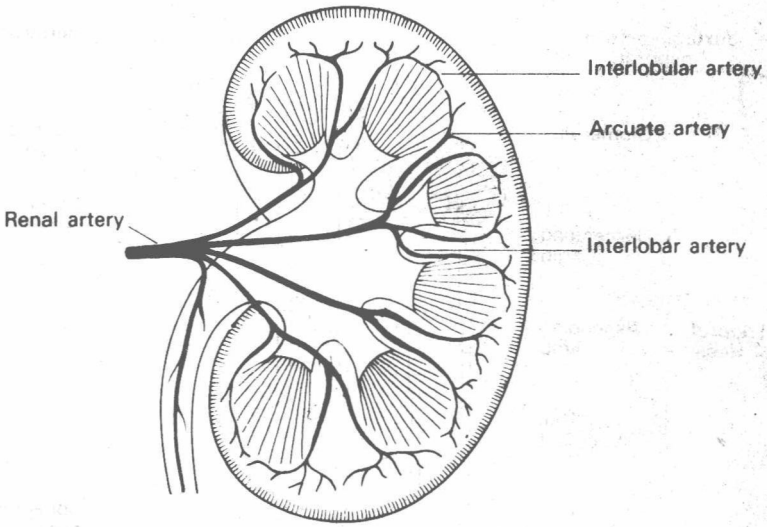

Fig. 2.3 Arterial supply to the kidney.

THE NEPHRON

Each kidney is composed of approximately 1 million functional units, known as nephrons. It is in these that blood is filtered and urine elaborated (Fig. 2.4).

Outer cortical nephrons have no loops of Henle and are concerned mainly with sodium regulation.

Inner cortical nephrons have long loops and are mainly concerned with the process of urinary concentration.

The nephrons are packed closely together in the kidney in such a way that adjacent structures tend to influence each other's function.

The structure and function of every component of the nephron is highly specialized.

The glomerulus

Glomerular capillaries arise from the afferent arteriole and terminate in the efferent arteriole. They develop *in situ* by differentiation of mesenchymal cells, situated in close proximity to the beginning of the tubular duct, culminating in an intricate branching network indenting Bowman's capsule (Fig. 2.5).

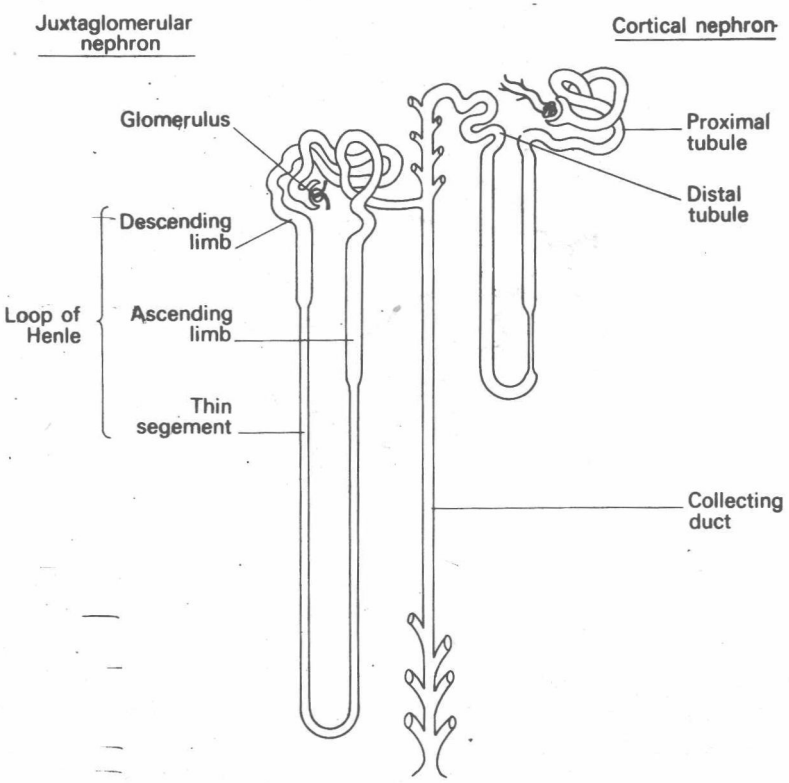

Fig. 2.4 The structure of the nephron.

The afferent arteriolar wall is a muscular structure. Those at the corticomedullary junction also possess cells which contain electron-dense granules and rough endoplasmic reticulum. These are the juxtaglomerular cells and they are thought to be the source of renin and possibly also of a sodium-regulating hormone.

The efferent arteriole is slightly narrower than the afferent and also has smooth muscle fibres in its wall.

Glomerular capillaries

They are composed of three layers—epithelium, basement membrane and endothelium (Fig. 2.6). In the central area of the glomerular tuft are the mesangium-containing cells.

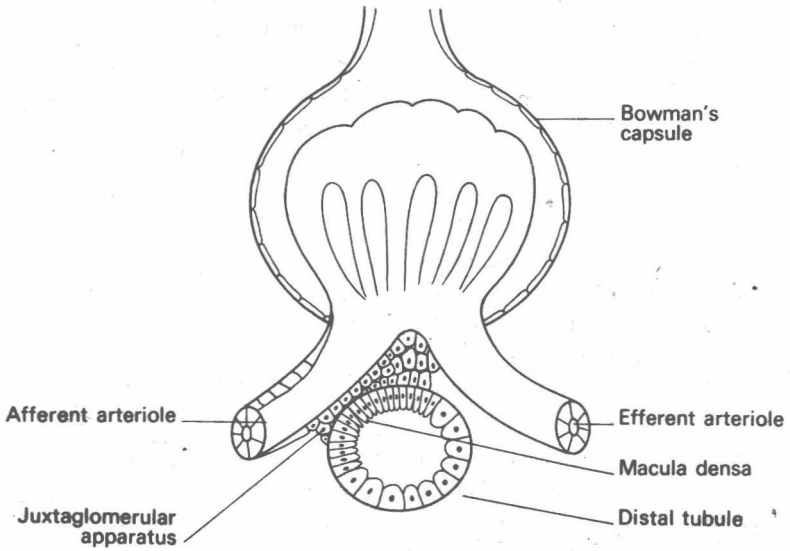

Fig. 2.5 The composition of the glomerulus.

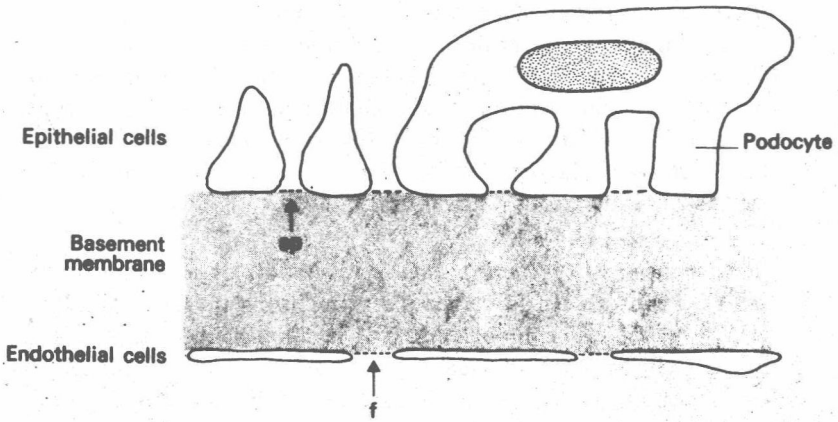

Fig. 2.6 The three layers of the glomerular capillary.

Endothelial cells are extensions of the afferent arteriolar endothelium. Numerous fenestrations (f) are present in them and these are bridged over by a thin diaphragm.

Basement membrane lies between endothelial and epithelial cells and is probably a homogeneous structure though a central denser region has been described. Its structure is ill defined but many people have suggested that it is composed of short delicate filaments arranged in an irregular meshwork similar to filter paper.

The epithelium is continuous with the parietal layer of Bowman's capsule. Each mature cell has a nucleus and long cell processes called podocytes (foot processes) which, in turn, are subdivided into smaller outgrowths or pedicels which interdigitate with each other and with similar pedicels from adjacent epithelial cells. The spaces between the pedicels are known as slit pores (sp) which are bridged by a thin filamentous membrane with a central thickening.

Mesangial cells are centrally situated in the glomerular tuft and are surrounded by matrix. They are considered to be of mesenchymal origin and when required they may develop into endothelial cells and, furthermore, may be capable of generating new basement membrane material. In some situations they may have phagocytic properties.

Proximal convoluted tubule is situated in the cortex. The epithelium is cuboidal and one layer deep. It has large basal nuclei—cell boundaries are irregular and interdigitated with boundaries of adjacent cells. The luminal surface has a brush border. The basal cell surface has many infoldings and high ATPase activity has been found in these regions. In the organ cells a Golgi zone surrounds the nucleus and there are numerous mitochondria.

The thin segment of Henle's loop is very short or absent in outer cortical nephrons. In juxtamedullary nephrons the loop descends into the medulla. The diameter is much less than that of the proximal tubule. Cells are flat and squamous and are star fish shaped; only a few mitochondria are present. Luminal surfaces have few short microvilli.

Distal tubule cells are cuboidal. Cytoplasma contains abundant rod-like mitochondria—mainly in the basal two-thirds of the cells and ribosomes. The nuclei are near the apex of the cell. The luminal

surface has short microvilli. The apices of the cells are pervaded by numerous tiny vesicles. The basal surfaces have many clefts (Fig. 2.7).

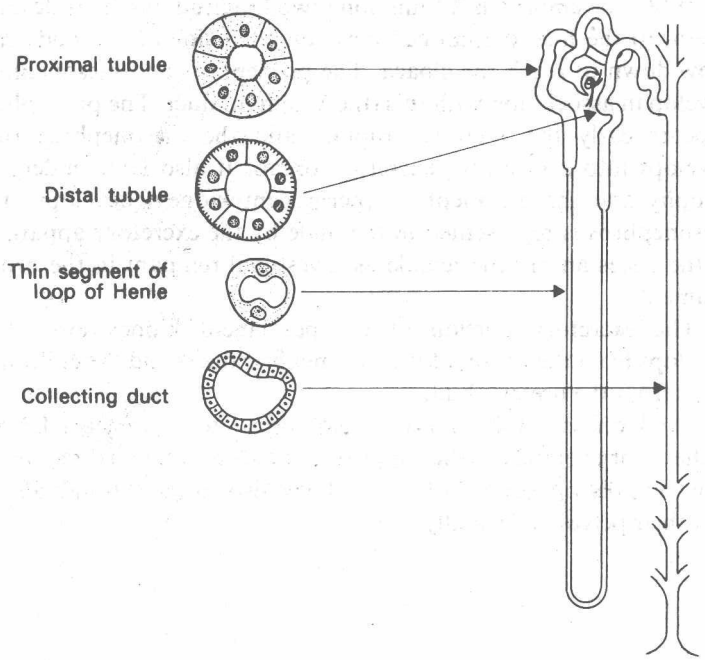

Fig. 2.7 Cross-sections of part of the cortical nephron.

Macula densa. When the distal tubule returns to the vicinity of its own glomerulus it makes a short tangiential contact with the afferent arteriole. At that point the tubular cells become narrow and the nuclei are densely crowded together. Mitochondria are scarce and round in shape (Fig. 2.5).

Collecting tubules contain cuboidal cells with only a few organelles. The luminal surface has short, coarse microvilli. The basal surface is smooth.

Pelvis, ureter and bladder have muscular walls which are lined by transitional epithelium.

EMBRYOLOGY

The basic elements of the kidney are derived from the mesoderm of the intermediate cell mass and the endoderm of the cloaca.

When the embryo is 2.5 mm long two longitudinal ducts develop lateral to the mesodermal cell mass on each side of the body and grow down to reach the cloaca. The pronephros and mesonephros develop in association with this (the Wolffian) duct. The pronephros appears early but regresses rapidly and the mesonephros then develops into a primitive excretory organ. It also later undergoes atrophy and the metanephros (permanent kidney) develops. The mesonephros is represented in the male by the excretory apparatus of the testes and in the female as a vestigial remnant in the broad ligament.

The excretory portion of the permanent kidney eventually develops from the fusion of the metanephric ducts and the collecting ducts from the ureteric bud.

The kidneys in the embryo develop opposite the vertebra L3 but as the embryo elongates they appear to move in a cranial direction to be eventually opposite D12 to L2. They also rotate through 90° so that their pelves lie medially.