Function of the nephron and the formation of urine

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Learning objectives

After reading this article, you should be able to:

- state the functions of the loop of Henlé
- explain how loop diuretics work
- list the components of the glomerular filtration barrier

Abstract

The nephron is the functional unit of the kidney involved in the critical interplay of fluid and electrolyte homeostasis by glomerular filtration, selective tubular reabsorption and secretion. This article will discuss the structure and function of each segment of the nephron, and the physiology pertaining to the formation of urine.

Keywords Bowman's capsule; collecting duct; distal convoluted tubule; juxtaglomerular apparatus; loop of Henlé; nephron; proximal convoluted tubule

Royal College of Anaesthetists CPD Matrix: 1A01

Introduction

The kidney is a multifunctional organ with a principle excretory role in the removal of nitrogenous waste products, toxins and metabolites, through the formation and excretion of urine. Other key functions of the kidney include: (1) regulation of water, electrolyte and inorganic ion balance; (2) maintaining acid–base homeostasis; (3) synthesis and secretion of hormones erythropoietin, renin, and 1,25-dihydroxycholecalciferol; and 4) gluconeogenesis.

Ultrastructure of the kidneys and renal vasculature

Detailing the anatomy of the nephron is essential to appreciate its physiological function. An adult kidney contains approximately 1–1.2 million functional nephrons. The functional unit of the kidneys is the nephron; a tubular structure composed of a single layer of epithelial cells. Each nephron consists of a *renal corpuscle* and associated *renal tubule* of contiguous segments. The tubule compromises the proximal convoluted tubule (PCT), loop of Henlé, distal convoluted tubule (DCT) and collecting duct system, which drains urine into the renal pelvis. The renal corpuscle is composed of two distinct structures, *Bowman's capsule*, a blind-ended tubule consisting of a single layer of epithelial cells and the *glomerulus*, a compact tuft of glomerular capillaries, which invaginates Bowman's capsule. The visceral layer of Bowman's capsule surrounds the globular network and reflects to become the parietal layer, forming the encasement of Bowman's capsule proper.

Urine formation commences with *glomerular filtration*; the passage of plasma from the glomerular capillaries into Bowman's space through the filtration barrier, comprised of the *capillary endothelium, glomerular basement membrane and podocyte layer*. The *capillary endothelium* forms a single cell layer around the glomerulus. The underlying *glomerular basement membrane* is a meshwork of structural glycoproteins, type IV collagen and proteoglycans. It consists of three layers: the thick central layer *lamina densa*, the *lamina rara interna* and the *lamina externa* supporting the podocyte layer. Podocytes are characterized by interdigiting cytoplasmic extensions, termed 'foot processes', enveloping around the capillaries. Gaps between their shorter processes are termed filtration slits, accounting as the chief filtration barrier of the glomerulus.

Nephrons are classified as *superficial cortical* or *juxtamedullary* nephrons, distinguished by the location of their glomeruli (Figure 1). The majority are cortical, the glomeruli of which are located in the renal cortex. Approximately 15% of nephrons are juxtamedullary with the renal corpuscle located near the corticomedullary junction. The juxtamedullary nephron has a higher glomerular filtration rate, as its associated glomerulus is proportionally larger than that of the cortical nephron. Furthermore, nephrons may be classified by the length of their respective loop of Henlé. Cortical nephrons have short loops of Henlé descending partially into the medulla, whereas most juxtamedullary loops extend to the inner medulla. This generates an osmotic gradient in the medulla.

The renal microvascular system is a complex portal circulation characterized by two independently regulated resistance vessels, the *afferent* and *efferent arterioles*. Blood enters the kidney via the renal artery, which branches into the interlobular artery, arcuate artery and cortical radial artery. Each glomerulus is supplied by an afferent arteriole, which exclusively filters up to 25% of a normal cardiac output. The afferent arteriole delivers blood to the first capillary network, the glomerular capillaries. The efferent arteriole carries blood to a second capillary network, the peritubular capillaries, which supply the nephron, before blood is collected by the renal venous system.

The vasculature of the juxtamedullary nephron differentiates from that of the cortical nephron, whereby specialized peritubular capillaries, the *vasa recta*, are closely associated with the loops of Henlé. The vasa recta function to maintain the hypertonic interstitial renal medulla to facilitate the concentration of urine.

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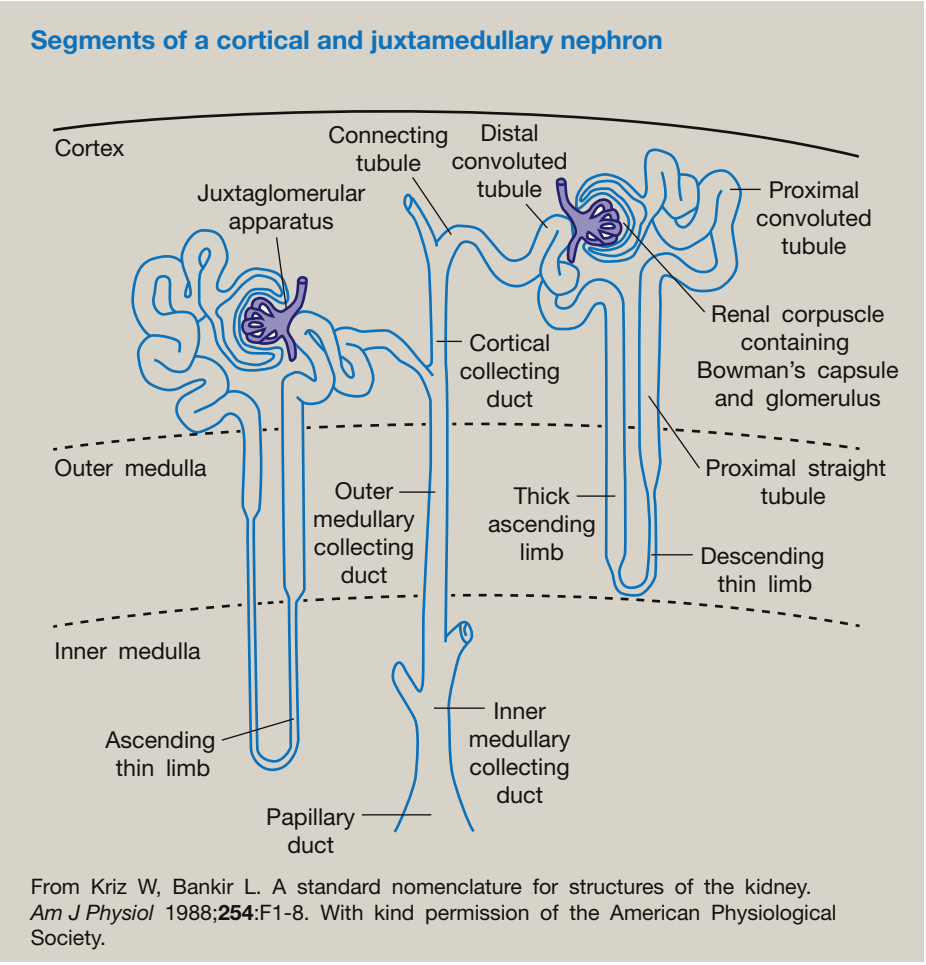

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Figure 1

The renal corpuscle

The renal corpuscle is the initial filtering component of the nephron. The passive process of 'ultrafiltration' from the glomerulus into Bowman's space is determined by all three layers of the renal corpuscle: the *capillary endothelium, glomerular basement membrane* and *podocyte layer*, which perform an important role as a selective filtration barrier.

Filtration is driven by the balance between hydrostatic and colloid osmotic pressures (Starling's forces) influenced by changes in vascular resistance due to the constriction of the efferent arteriole compared to the afferent arteriole. The differential resistance and hence filtration may be modulated by sympathetic nerve activity, vasoconstrictors and vasodilators. The kidney glomerulus is responsible for filtration of approximately 20% of plasma into Bowman's capsule through semi-permeable vessels of the glomerular tuft.

Mesangial cells are modified smooth muscle cells, which structurally support the glomerular capillary loops. Their contractile activity is postulated to influence the glomerular filtration rate by decreasing the ultrafiltration coefficient through a decrease in capillary surface area and capillary permeability. Furthermore, they have a known secretory role to produce growth factors and proteins in normal glomerular development and in phagocytosis.

Podocytes are a major component of the filtration barrier. Their unique structure consists of major processes extending from their cell body to form interdigiting foot processes to entwine glomerular capillaries. Filtration slits in-between opposing foot processes prevent plasma proteins from entering the glomerular ultrafiltrate and further participate in podocyte signalling. A negatively charged coat of glycoproteins (glycocalyx) encase the foot processes and slit diaphragm, attributing to negative surface charges throughout the glomerular filtration barrier, maintaining the architecture of podocytes by electrostatically repelling adjacent foot processes. The fenestrated endothelium resting upon the glomerular basement membrane is densely perforated facing the urinary space.

These three components of the glomerular filtration barrier permit the passage of macromolecules determined by: (1) size; (2) charge; and (3) configuration. Cells with a larger molecular weight, such as albumin (MW 68,000) are retained, whereas smaller molecules such as haemoglobin may pass freely. Retention of larger molecules further controls water flow by exerting a colloidal osmotic pressure. The negative charge of the capillary endothelium and lamina rara inhibit passage of anionic

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