The excretory process, while universal among eukaryotes, is the removal of materials from the body. The predominant function of the kidney is excretion, which is broadly defined as the removal of materials from the body. The excretory process, while universal among fish, can vary tremendously with respect to the volume and chemical composition of the excretory fluid (urine) produced, as well as the mechanisms leading to urine formation. For example, fish inhabiting a freshwater (FW) environment produce large volumes of dilute urine to rid the body of water absorbed at the gill without unduly exacerbating net salt loss. On the other hand, seawater (SW) teleost fish produce small quantities of isosmotic urine to conserve water and to eliminate salts in the face of continual branchial passive water loss and salt gain. In most fish, urine formation is the net result of glomerular filtration, fluid and solute reabsorption, and secretion. However, a number of SW species possess aglomerular kidneys and thus produce urine exclusively by tubular secretion. This is but one example of the enormous functional and phenotypic diversity surrounding the fish kidney that make it such an excellent model for studying structure–function relationships in piscine physiological systems.

## Kidney Structure

### Aglomerular Kidneys

Approximately 40 species of fish are known to possess aglomerular (lacking glomeruli) kidneys representing a mere 0.1% of extant fish species. Aglomerularism evolved independently from glomerular ancestors at least four times during the teleostean phylogeny. Examples of fish with aglomerular kidneys are toadfish (family Batrachoididae), goosefish and anglerfish (family Lophiidae), pipefish and seahorses (family Syngnathidae), some pufferfish (family Tetraodontidae) and some Antarctic icefishes (family Nototheniidae), among others. Not only do the kidneys of these fish lack glomeruli, also they often do not possess distal tubules. Thus, the basic structure of the aglomerular nephron consists of a proximal portion resembling the second proximal segment of the teleost glomerular kidney (see below) and a collecting duct system. As the distal tubule is crucial for the production of dilute urine, the aglomerular kidney is limited in its capacity to accommodate fluid loads because the lower limit of urine osmolarity is believed to be approximately 200 mOsm L^{-1}. Thus, the renal excretion of a large fluid load would also be accompanied by significant loss of salt. It is probably for this reason, rather than the absence of glomeruli, per se, that aglomerular fish are restricted to the SW or estuarine environment.

### Glomerular Kidneys

Majority of fishes have what is termed a glomerular kidney. Glomerular kidneys share the common function of producing urine through a first step of ultrafiltration at the glomerulus (a network of capillaries contained within Bowman’s capsule). Beyond this one common feature, however, glomerular kidneys exhibit substantial anatomical variation among the fish groups.

---

**Glossary**

- **Acid–base balance** The regulation of constant pH in the body compartments usually achieved by adjustments of \( P_{\text{CO}_2} \) and/or \( \text{HCO}_3^- \) levels.
- **Glomerular ultrafiltration** The process whereby blood plasma is filtered at the glomerulus to produce the primary urine which is subsequently modified by secretion and reabsorption.
- **Glucosuria** The presence of abnormally elevated levels of glucose in the urine.
- **Hypercapnia** High levels of carbon dioxide in blood.
- **Mesangial cell** A renal cell type that contacts the endothelial cells of the glomerulus and thus constitutes a portion of the filtration barrier.
- **Pedicel** The extended projections arising from podocytes that interdigitate to form filtration slits.
- **Podocyte** Cells of the renal visceral epithelium that form a critical component of the glomerular filtration barrier, contributing size selectivity and maintaining a large filtration surface.
- **Tubular transport maximum** The maximal rate at which a substance can be reabsorbed (or secreted) by the kidney.
Cyclostomes
Adult hagfish possess two discrete kidneys (pronephric and mesonephric); however, only the posterior mesonephric kidney, a paired elongated structure lying on either side of the midline, is believed to be functional. Each side of the hagfish mesonephric kidney contains about 40 nephrons that drain into paired mesonephric ducts (ureters). The ultrafiltrate produced by glomerular filtration within Bowman’s capsule enters a short neck segment prior to delivery into the mesonephric duct. The epithelial cells lining the mesonephric duct resemble the cells of the first proximal segment of the teleost nphron (see below). The kidney of lampreys, as in hagfish, is a paired, elongated structure. However, in most other respects, the lamprey kidney bears little resemblance to the hagfish nphron but more closely resembles the kidneys of the more advanced teleosts. Thus, the glomerulus is followed by a short neck segment, a proximal tubule, an intermediate segment, a distal tubule, and a collecting duct which empties into a mesonephric duct.

Elasmobranchs
The elasmobranch nphron is by far the most elaborate within the various fish taxa and, in some respects, is similar to the mammalian kidney because of the occurrence of countercurrent tubular flow. The tubules form two loops with limbs that descend and ascend in countercurrent parallel pathways through two discrete zones, a bundle zone and a sinus zone. The bundle zone is encapsulated by a peritubular sheath that may allow control over the chemical composition of the interstitial fluid and possibly assist urea and trimethylamine oxide (TMAO) reabsorption via countercurrent multiplication.

Teleosts
The teleost kidney contains two sections: a head kidney, which comprises about 20% of the anterior portion of the kidney and the trunk kidney which comprises the other 80% and extends along the dorsal wall of the body cavity. The head kidney is largely composed of steroidogenic interrenal cells, chromaffin cells, and hematopoietic tissue while the trunk kidney contains the vast majority of filtering nephrons in addition to hematopoietic and pigmented cells. The teleost kidney is typically grouped into three functional categories (FW, SW, and euryhaline) and into five anatomical classes (types I–V). The distinction of the five classes is based largely on the extent of separation between the trunk and head kidney and the degree of fusion of the left and right kidneys. For example, nearly all marine species are grouped within category III in which only the posterior portion of the kidney is fused and the anterior region is composed of two slender branches. There are relatively few anatomical differences in the tubular composition of FW, SW, and euryhaline fishes with all of them possessing a neck segment exiting Bowman’s capsule, two segments of proximal tubule, and a collecting duct. The collecting ducts drain into two mesonephric ducts, which fuse to form a common archinephric duct (bladder). The FW nphron, which is designed to produce large volumes of dilute urine, has large glomeruli and a distal tubule which is essential for NaCl reabsorption and the production of dilute urine. The FW nphron also contains an intermediate segment positioned between the proximal and distal tubules; the function of the intermediate segment is unknown. The nphron of euryhaline species also contains a distal tubule, but its role in NaCl reabsorption varies according to salinity. The marine nphron which is designed for water conservation possesses smaller glomeruli and usually lacks the diluting distal tubule (Fig. 1).

Urine Formation
In the glomerular kidney, urine is formed through the interactive effects of ultrafiltration, water and solute reabsorption, and secretion. This strategy allows great flexibility in the chemical composition of the final urine that is excreted because the primary urine (ultrafiltrate) can be extensively and variably modified by reabsorption and secretion (Fig. 2).

Ultrafiltration
Ultrafiltration is the process whereby blood plasma is selectively filtered at the glomerulus to produce the primary urine in an epithelial-lined tubule. The process of glomerular ultrafiltration is driven by pressure gradients across a filtration barrier within the glomerulus, which is composed of the capillary endothelium, a matrix of mesangial cells, a basement membrane, and a visceral epithelium. The visceral epithelium is composed of podocytes that give rise to cellular projections termed pedicels, which can be arranged to form slits through which filtration occurs. As in other kidneys, two types of pressure determine the net filtration pressure. A positive hydrostatic pressure difference between glomerular capillaries and the lumen of Bowman’s capsule generates filtration across the filtration barrier. A countereacting negative colloid osmotic pressure difference opposes filtration. The hydrostatic pressure in the glomerular capillaries is largely dictated by the blood pressure in the glomerular capillaries, which is greatly influenced by variations in cardiac output and the vascular resistance in the afferent and efferent renal arterioles. The colloid osmotic pressure difference arises because the filtrate formed within Bowman’s capsule is largely devoid of protein. Net filtration along the length of glomerular capillaries persists as long as hydrostatic pressure exceeds plasma colloid osmotic pressure. However, as fluid is lost from glomerular capillaries by filtration, colloid osmotic pressure increases and hydrostatic pressure decreases (very slightly) until net filtration pressure falls to zero. Consequently, the process of ultrafiltration produces primary urine which, except for its lack of protein, has a chemical composition similar to plasma (Fig. 3).
Within any given nephron, the rate at which the ultrafiltrate is formed is termed the single nephron glomerular filtration rate (SNGFR), which is determined by pressure gradients, hydraulic conductivity, and the surface area over which filtration is occurring. The glomerular filtration rate (GFR) for the entire kidney is set by the number of filtering nephrons and their SNGFRs. Urine flow rate, which can be highly variable in FW fish, is always less than GFR because of tubular reabsorption; but since fractional tubular reabsorption tends to be held constant, GFR and urine flow rate tend to be proportional. Typically, a small fraction of nephrons are...
unperfused and thus do not contribute to urine formation. Moreover, not all of the perfused nephrons are actually filtering at any given time. Thus, GFR can be rapidly modified by glomerular recruitment (or de-recruitment), whereby the numbers of filtering nephrons are adjusted.

The principal factors contributing to glomerular recruitment are changes in arterial blood pressure and renal blood flow. Factors contributing to increased systemic arterial blood pressure, such as circulating catecholamines or activation of sympathetic nerve fibers, will promote glomerular recruitment, besides increasing SNGFR (assuming no changes in renal blood-flow patterns). Angiotensin II, the product of the renin-angiotensin-system (RAS), while promoting an elevation of systemic blood pressure, actually acts as an antidiuretic (reduces urine formation) in fish because of its vasoconstrictory actions on the afferent renal vasculature and its effects on glomerular ultrastructure.

The lower urine flow rates in SW fish or in euryhaline fish experiencing increasing environmental salinity are predominantly related to marked reductions in GFR. In SW fish, the reduced GFR primarily reflects anatomical changes – fewer and smaller glomeruli as well as alterations in their morphology that promote a reduced hydraulic permeability. For example, the pedicels, which are arranged to form leaky filtration slits in FW fish, are either poorly developed or tightly packed together to limit filtration. In addition, the podocytes overlying the glomerular capillaries are more sparsely distributed in FW fish, while they tend to be more abundant and flattened in SW fish to further limit filtration.

Reabsorption

Depending on species and environmental salinity, fractional reabsorption may be entirely absent (hagfish) or as high as 97% (FW teleosts). While impressive in FW teleosts, the capacity of the fish kidney to reabsorb filtered NaCl remains considerably less than in the mammalian nephron where ~99% of the filtered NaCl is reabsorbed. Moreover, unlike in mammals where the bulk of NaCl reabsorption occurs at the proximal tubule, fish appear to rely at least equally on segments distal to the proximal tubule. For example, in the lamprey (*Lampreta fluviatilis*) only 10% of filtered NaCl is reabsorbed at the proximal tubule, while 80% is reabsorbed at the collecting duct.

Fig. 3  Structure of the teleost glomerular kidney. (a) A corrosion cast of a glomerulus with single afferent (A) and efferent (E) arterioles. Arrow indicates endothelial cell indentations. Asterisks show positions of origin and end of afferent arteriole used to measure the length of the vessel. (b) A transmission electron micrograph of the glomerular capillary wall in an FW trout; capillary endothelium (End), mesangial matrix (M), basement membrane (B), visceral epithelium (Ep). Epithelial pedicels (Pe) are connected by slit diaphragms. (c) Visceral epithelium of glomerulus of an FW trout showing rounded epithelial podocytes (P) with primary processes, sometimes branching into secondary and tertiary processes (large arrows) and terminating in pedicels (small arrows). An area of regular interdigitation of pedicels is enclosed by dotted outline. Some pedicels arise directly from podocytes (arrowheads). Few cytoplasmic microprojections present on podocyte and its processes. (d) Seawater adapted fish. Flattened podocytes and broad, flat primary processes (large arrows) with little visible interdigitation of pedicels. Many cytoplasmic microprojections (small arrows). Bar=(a) 20 μm; (b) ~1 μm; (c) ~4 μm; and (d) 4 μm. (a) Reproduced from Brown, J.A., 1985. Renal microvasculature of the rainbow trout, *Salmo gairdneri* – Scanning electron-microscopy of corrosion casts of glomeruli. Anatomical Record 213(4), 505–513. (b)–(d) Reproduced from Brown, J.A., Taylor, S.M., Gray, C.J., 1983. Glomerular ultrastructure of the trout, *Salmo gairdneri* – Glomerular capillary epithelium and the effects of environmental salinity. Cell and Tissue Research 230(1), 205–218.
In teleosts, the predominant solutes reabsorbed from the primary urine are Na\(^+\), Cl\(^-\), Ca\(^{2+}\), and glucose. For NaCl, the greatest rates of reabsorption are found in FW species because of their need to produce dilute urine (ie, retain salt but lose excess water). Correspondingly, relatively little water is reabsorbed. Typically, less than 50% and occasionally as little as 5% of the filtered water is reabsorbed.

The mechanisms of Na\(^+\) and Cl\(^-\) reabsorption are not well understood. Na\(^+\) uptake from the filtrate probably involves electroneutral Na\(^+\)/H\(^+\) exchange via one or more members of the SLC9 family of Na\(^+\)/H\(^+\) exchangers (eg, NHE3 and NHE2), while Cl\(^-\) uptake may be achieved by Cl\(^-\)/HCO\(_3\)\(^-\) exchange via members of the SLC4 (eg, SLC4A2) and SLC26 (eg, SLC26A4 and SLC26A6) anion transporter gene families. An essential driving force for trans-tubular Na\(^+\) uptake is basolateral Na\(^+\)/K\(^+\)-ATPase (NKA), which facilitates the final re-entry step of Na\(^+\) into the blood. The tubular reabsorption of Ca\(^{2+}\) is thought to involve its passive entry across the luminal (mucosal) membrane through an epithelial Ca\(^{2+}\) channel (ECaC) followed by active transport across the serosal membrane via Ca\(^{2+}\)-ATPase (PMCA).

The teleost nephron, like the mammalian kidney, has an excellent capacity to reabsorb dissolved glucose lost to the filtrate; virtually all glucose is removed from the filtrate under normal conditions. In rainbow trout, the predominant mechanism of glucose reabsorption is via coupled Na\(^+\)–glucose transporters. The tubular transport maximum for glucose (TmG) in the trout kidney is about 150 μmol kg\(^{-1}\) h\(^{-1}\), which corresponds to plasma glucose levels exceeding 20 mM. Thus, it is unlikely that significant glucose will be lost in the urine (a condition termed glucosuria) except after acute dietary carbohydrate loading.

### Secretion

In addition to ultrafiltration, solutes can be removed from the blood and they can enter the urine by secretion; examples of secreted solutes include Ca\(^{2+}\), Mg\(^{2+}\), NH\(_4\)\(^+\), H\(^+\), K\(^+\), SO\(_4\)\(^{2-}\), and PO\(_4\)\(^{3-}\). To determine whether or not a solute is undergoing net secretion, the renal clearance ratio (RCR) for that solute must be determined. The RCR is the ratio of the amount of solute excreted in the urine (UFR \(\times\) urine (solute)) to the amount filtered (GFR \(\times\) plasma (solute)). If the RCR exceeds 1 (excretion exceeds filtration), this indicates net secretion into the urine whereas a RCR less than 1 indicates net reabsorption. It is important to emphasize that the RCR provides data only on the net tubular processes. RCR only reveals which processes dominate in cases where solutes are reabsorbed as well as secreted (eg, K\(^+\) and Ca\(^{2+}\)).

In FW fish, the extent of tubular secretion for any given secreted ion essentially reflects the blood chemistry, which in turn is largely controlled by dietary loading and acid–base status. For example, dietary ingestion of Mg\(^{2+}\) and SO\(_4\)\(^{2-}\) will promote increased secretion of these solutes, while catabolism of ingested protein to ammonia will promote NH\(_4\)\(^+\) secretion. Acidification of the blood may be associated with increased secretion of H\(^+\) (see below), which in turn may be associated with markedly increased secretion rates of PO\(_4\)\(^{3-}\) and NH\(_4\)\(^+\). SW fish secrete significant quantities of divalent ions which are largely derived from ingested seawater. The nature of divalent ion secretion is poorly understood but may involve Mg\(^{2+}\)/Na\(^+\) exchange, Mg\(^{2+}\)/H\(^+\) exchange, and anion/SO\(_4\)\(^{2-}\) exchanges (possibly via SLC26A1).

### Acid–Base Balance by the Kidney

Although the gill is the predominant site of acid–base regulation in fish, the kidney also plays an essential role that should not be underestimated. Fish regulate blood pH through modulations of plasma HCO\(_3\)\(^-\) levels, which in turn are dictated by adjustments of branchial acid excretion. For example, the regulation of respiratory acidosis is associated with marked increases in plasma HCO\(_3\)\(^-\) levels which may routinely exceed 20 mM and even reach values exceeding 70 mM (eg, in European eel, Anguilla anguilla exposed to an external P\(_{CO_2}\) of 45 mmHg). Under such conditions, it is essential that the kidney is able to reabsorb the filtered HCO\(_3\)\(^-\). Essentially, branchial acid excretion would become a futile exercise in the absence of a renal mechanism for the retention of accumulated HCO\(_3\)\(^-\) ions. Thus, for every additional mol of HCO\(_3\)\(^-\) appearing in the glomerular filtrate, the kidney must secrete an additional mol of H\(^+\) to ensure complete HCO\(_3\)\(^-\) reabsorption. As increases in renal acid secretion are effectively used to reabsorb excess filtered HCO\(_3\)\(^-\), it is rare that net acid excretion by the kidney will ever match the markedly elevated rates of acid excretion occurring at the gill during compensation of acidosis. On the other hand, the rates of renal acid secretion required to sustain a condition of fully compensated respiratory acidosis (ie, elevated HCO\(_3\)\(^-\) to achieve normal pH at high P\(_{CO_2}\)) are likely to approach the rates of peak acid excretion at the gill. It is important to emphasize that under conditions of chronic hypercapnia, high rates of renal acid secretion must be sustained whereas the elevation of branchial acid excretion need last only as long as it takes to accumulate sufficient HCO\(_3\)\(^-\) to raise pH back to normal.

The potential for renal mechanisms to contribute to acid–base regulation appears to be highest in FW fish, where large volumes of urine are produced (see above). In SW fishes, the pH-regulating capacity of the kidney is limited by low urine flow rates and an apparent lack of responsiveness to systemic acid–base disturbances. By contrast, the responses of the FW teleost kidney to acid–base disturbances are comparable in pattern and flexibility to those of the mammalian kidney, although quantitatively subservient to those of the gill (although see above).

Previous work suggests that the mechanism of renal HCO\(_3\)\(^-\) reabsorption in rainbow trout in many ways parallels that of the mammalian proximal tubule, the site responsible for 80–90% of renal HCO\(_3\)\(^-\) reabsorption in mammals (Fig. 4).
Acid secretion into the filtrate across the luminal membrane is achieved via two mechanisms: electroneutral Na\(^+\)/H\(^+\) exchange and active H\(^+\) pumping by V-type H\(^+\)-ATPase. In rainbow trout, the specific Na\(^+\)/H\(^+\) exchanger thought to be involved in renal acid secretion is NHE3 or SLC9A3. H\(^+\) ions secreted into the filtrate combine with HCO\(_3^-\)/CO\(_3^-\) to form CO\(_2\), a reaction catalyzed by membrane-associated carbonic anhydrase isoform IV (tCA IV). The CO\(_2\) diffuses into the tubule cells where it is dehydrated to HCO\(_3^-\)/CO\(_3^-\) in the presence of cytosolic carbonic anhydrase (tCAc). The H\(^+\) ions thus formed re-enter the filtrate via NHE3 or H\(^+\)-ATPase while the HCO\(_3^-\)/CO\(_3^-\) is reabsorbed into the plasma via Na\(^+\)–HCO\(_3^-\)/CO\(_3^-\) co-transporter isoform 1 (NBC1) (Figs. 5–7).

**Nitrogen Excretion by the Kidney**

The two predominant forms of nitrogenous waste excreted in the urine are ammonia and urea with negligible contributions from other N\(_2\)-containing substances such as uric acid, creatine, and creatinine. It is important to point out that the rates of renal ammonia and/or urea excretion, while substantial, comprise only a small fraction (<5%) of whole-body nitrogen excretion. Although increasing the rates of renal ammonia excretion will not markedly affect whole-body N\(_2\) balance, it can have a significant consequence on renal acid–base balance because ammonia is an important urinary buffer. Ultimately, the capacity of the urine to excrete acid is related to the presence of buffers such as ammonia and phosphate. In the ureogenic marine elasmobranchs that...
accumulate high levels of urea in the blood as an osmolyte, the role of the kidney is to ensure that filtered urea is effectively reabsorbed. The mechanism of reabsorption of urea by the elasmobranch kidney likely involves a facilitated urea transporter which has been cloned and characterized in dogfish.

Further Reading


