

William H. Dantzler

Comparative Physiology of the Vertebrate Kidney

Second Edition

*Published on behalf of The American
Physiological Society by Springer*



 Springer

Comparative Physiology of the Vertebrate Kidney

Published on behalf of The American Physiological Society
by Springer

This book is published on behalf of the American Physiological Society (APS) by Springer. Access to APS books published with Springer is free to APS members.

APS publishes three book series in partnership with Springer: *Physiology in Health and Disease* (formerly *Clinical Physiology*), *Methods in Physiology*, and *Perspectives in Physiology* (formerly *People and Ideas*), as well as general titles.

William H. Dantzler

Comparative Physiology of the Vertebrate Kidney

Second Edition



Springer



William H. Dantzer
Department of Physiology
University of Arizona, College of Medicine
Tucson, Arizona
USA

The first edition was published as volume of the book series “Zoophysiology”.

ISBN 978-1-4939-3732-5 ISBN 978-1-4939-3734-9 (eBook)
DOI 10.1007/978-1-4939-3734-9

Library of Congress Control Number: 2016940048

1st edition: © Springer-Verlag Berlin Heidelberg 1989

2nd edition: © The American Physiological Society 2016

This work is subject to copyright. All rights are reserved by the Publisher, whether the whole or part of the material is concerned, specifically the rights of translation, reprinting, reuse of illustrations, recitation, broadcasting, reproduction on microfilms or in any other physical way, and transmission or information storage and retrieval, electronic adaptation, computer software, or by similar or dissimilar methodology now known or hereafter developed.

The use of general descriptive names, registered names, trademarks, service marks, etc. in this publication does not imply, even in the absence of a specific statement, that such names are exempt from the relevant protective laws and regulations and therefore free for general use.

The publisher, the authors and the editors are safe to assume that the advice and information in this book are believed to be true and accurate at the date of publication. Neither the publisher nor the authors or the editors give a warranty, express or implied, with respect to the material contained herein or for any errors or omissions that may have been made.

Printed on acid-free paper

This Springer imprint is published by Springer Nature
The registered company is Springer Science+Business Media LLC New York

Preface

Like the first edition, this new edition emphasizes the comparative approach to understanding vertebrate renal function. I remain convinced that this approach is of particular value in understanding both the details of renal function at the cellular and molecular levels and the renal role in regulating vertebrate fluid volumes and solute concentrations. My exposure to this approach first occurred during a student research experience in the laboratory of the late Wilbur H. Sawyer, who also provided an introduction to the works of Homer W. Smith and August Krogh. The importance of this approach was reinforced by doctoral and postdoctoral research in the laboratory of the late Bodil Schmidt-Nielsen. It has been confirmed through years of personal experience since then.

My research and my understanding of renal function have been aided through the years by collaboration and discussion with numerous students and postdoctoral associates. Of particular importance in developing my views on comparative renal function, on the relationship of renal structure to function, and on transport processes have been my long-term associations with my colleagues and friends, Eldon J. Braun, Thomas L. Pannabecker, and Stephen H. Wright at the University of Arizona; Stefan Silbernagl at the University of Würzburg, Würzburg, Germany; and Varanuj Chatsudthipong at Mahidol University, Bangkok, Thailand. Much of my personal research over the years has been supported by grants from the United States National Science Foundation and National Institutes of Health.

I thank my fellow scientists for sometimes allowing me to note their unpublished observations. I also thank them and their publishers for permitting me to use many published figures. Finally, and most importantly, I thank my wife, Barbara, not only for enduring my absorption with my work but also for providing the constant encouragement and support that has so greatly aided my progress.

Tucson, AZ
Spring, 2016

William H. Dantzler

Contents

1	Introduction	1
1.1	The Comparative Approach	1
1.2	Environmental Requirements in Regulating the Water and Solute Composition of the Internal Environment	2
1.3	Possible Roles of Kidneys in Regulating Water and Solute Composition of the Internal Environment	2
1.4	Useful Reviews on Comparative Renal Physiology	4
	References	4
2	Renal Morphology	7
2.1	Introduction	7
2.2	Gross External and Internal Morphology	8
2.2.1	General Considerations	8
2.2.2	Fishes	10
2.2.3	Amphibians	14
2.2.4	Reptiles	15
2.2.5	Birds	16
2.2.6	Mammals	19
2.2.7	General Blood Vessel Patterns	21
2.3	Fine Internal Structure	23
2.3.1	General Considerations	23
2.3.2	Glomerulus	24
2.3.3	Proximal Tubule	27
2.3.4	Early Distal Tubule	28
2.3.5	Late Distal and Collecting Tubules	29
2.3.6	Juxtaglomerular Apparatus	32
	References	33
3	Initial Process in Urine Formation	37
3.1	Introduction	37

- 3.2 Filtration of Fluid by Glomeruli 38
 - 3.2.1 Process of Ultrafiltrate Formation at Renal Glomeruli 38
 - 3.2.2 Values for Single-Nephron Glomerular Filtration Rates 45
 - 3.2.3 Changes in Whole-Kidney Glomerular Filtration Rates 46
 - 3.2.4 Changes in Single-Nephron Filtration Rates and in Number of Filtering Nephrons 51
 - 3.2.5 Regulation of Single-Nephron Glomerular Filtration Rates and Number of Filtering Nephrons 59
- 3.3 Filtration of Protein by Glomeruli 69
- 3.4 Secretion of Fluid by Tubules 71
- References 72
- 4 Transport of Inorganic Ions by Renal Tubules 81**
 - 4.1 Introduction 81
 - 4.2 Sodium and Chloride 82
 - 4.2.1 Direction, Magnitude, and Sites of Net Transport 82
 - 4.2.2 Mechanism of Transport 88
 - 4.2.3 Regulation of Transport 105
 - 4.3 Potassium 113
 - 4.3.1 Direction, Magnitude, and Sites of Transport 113
 - 4.3.2 Mechanism of Transport 114
 - 4.3.3 Hormonal Regulation 117
 - 4.4 Hydrogen Ion 120
 - 4.4.1 Magnitude and Sites of Net Transport 120
 - 4.4.2 Mechanism of Transport 121
 - 4.5 Calcium 125
 - 4.5.1 Direction, Magnitude, and Sites of Transport 125
 - 4.5.2 Mechanism of Transport 126
 - 4.5.3 Hormonal Regulation 128
 - 4.6 Phosphate 130
 - 4.6.1 Direction, Magnitude, and Sites of Net Transport 130
 - 4.6.2 Mechanism of Transport 131
 - 4.6.3 Hormonal Regulation 134
 - 4.7 Magnesium 138
 - 4.7.1 Direction, Magnitude, and Sites of Net Transport 138
 - 4.7.2 Mechanism of Transport 139
 - 4.8 Sulfate 141
 - 4.8.1 Direction, Magnitude, and Sites of Net Transport 141
 - 4.8.2 Mechanism of Transport 142
- References 143

5	Transport of Fluid by Renal Tubules	159
5.1	Introduction	159
5.2	Fluid Reabsorption	160
5.2.1	Magnitude and Sites of Net Reabsorption	160
5.2.2	Mechanism and Control of Fluid Reabsorption	163
5.3	Fluid Secretion	168
	References	169
6	Transport of Organic Substances by Renal Tubules	173
6.1	Introduction	173
6.2	Glucose	174
6.2.1	Direction, Magnitude, and Sites of Transport	174
6.2.2	Mechanism of Transport	176
6.3	Bicarbonate	180
6.3.1	Direction, Magnitude, and Sites of Transport	180
6.3.2	Mechanism of Transport	182
6.4	Amino Acids	184
6.4.1	Direction, Magnitude, and Sites of Net Transport	184
6.4.2	Mechanism of Transport	185
6.5	Urea	189
6.5.1	Direction, Magnitude, and Sites of Net Transport	189
6.5.2	Mechanism of Transport	192
6.6	Ammonia	196
6.6.1	Magnitude and Sites of Net Secretion	196
6.6.2	Process of Production and Secretion	198
6.7	Organic Anions and Acids (Except Amino Acids, Urate, and Lactate)	202
6.7.1	Direction and Sites of Net Transport	202
6.7.2	Mechanism of Transport	203
6.8	Urate	210
6.8.1	Direction, Magnitude, and Sites of Net transport	210
6.8.2	Mechanism of Transport	211
6.9	Lactate	218
6.10	Organic Cations and Bases	219
6.10.1	Direction and Sites of Net Transport	219
6.10.2	Mechanism of Transport	220
	References	224
7	Diluting and Concentrating Mechanism	237
7.1	Introduction	237
7.2	Range of Urine Osmolality	238
7.3	Process and Sites of Dilution	244
7.4	Process of Concentration	245
7.5	Regulation of Urine Osmolality	253
	References	258

8	Integrative Summary of Renal Function	263
8.1	Introduction	263
8.2	Integrative Summary Within Each of the Major Vertebrate Groups	264
8.2.1	Fishes	264
8.2.2	Amphibians	268
8.2.3	Reptiles	270
8.2.4	Birds	272
8.2.5	Mammals	274
8.3	Summary Comparisons and Contrasts of Renal Function Between Groups of Vertebrates	275
8.3.1	Glomerular Filtration Rate: Stability Versus Lability	275
8.3.2	Diluting and Concentrating Processes	277
8.3.3	Sites and Mechanisms of Tubular Transport	279
	Index	283

Chapter 1

Introduction

Abstract This chapter points out the general importance of the kidney in regulating the internal environment of all vertebrates. It then discusses the importance of the comparative approach in understanding renal physiology. Next, it briefly indicates the environmental requirements and the possible roles of the kidney in regulating the water and solute composition of the internal environment. Finally, it suggests some possible useful reviews on comparative renal physiology.

Keywords Kidney importance • Comparative approach • Internal environment • Water • Solutes • Regulation • Published reviews

Kidneys play a role—usually a major role—in regulating water and solute composition of the internal environment of all vertebrates. In this book, I examine the physiological functions of the kidneys from a comparative viewpoint with emphasis on nonmammalian vertebrates. I consider mammalian renal function for comparison with nonmammalian renal function and as a frame of reference for some discussions. However, I make no attempt to consider the vast literature on mammalian renal function in detail. In fact, I do not give the studies on nonmammalian vertebrates in complete detail. Instead, I summarize primarily the major findings and the important unanswered questions raised by those findings, for I do not intend this volume as an all-inclusive reference. I intend it as a reasonably comprehensive and integrated picture of comparative renal function for the biological scientist or advanced student of biology who has some knowledge of physiology and a desire to know more about renal function in vertebrates and for the mammalian renal physiologist who wishes to obtain a broader view of renal function. I hope that some of these readers will be sufficiently intrigued by the many unsolved problems of renal function in nonmammalian vertebrates that they will try to solve them with modern techniques and new experimental designs.

1.1 The Comparative Approach

The comparative approach to understanding renal function has a number of advantages. First, a consideration of those physiological processes that make it possible for different species to survive under diverse environmental conditions not only

increases our understanding of environmental adaptations but also may suggest those scientific studies most likely to reveal important general physiological principles. Second, the comparison of renal function in a variety of species often permits the exploration of a basic physiological mechanism in an exaggerated form in a single species (August Krogh principle) (Krogh 1929) or through the use of a simple preparation.

The comparative approach to physiological studies has often been suggested as a means of shedding light on the evolution of physiological processes. However, the information available on renal function in nonmammalian vertebrates is so fragmented and so frequently limited to a single species or a few species and so seldom involves genetic details that attempts to reach major conclusions about evolution of mechanisms result only in unwarranted speculation. Therefore, although I make comparisons of renal mechanisms and adaptations among the major vertebrate groups throughout the book, particularly in Chap. 8, and I occasionally note the apparent independent evolution of comparable mechanisms in separate vertebrate groups (e.g., the mechanism for concentrating the urine in birds and mammals), I avoid general conclusions about the phylogenetic evolution of renal mechanisms.

1.2 Environmental Requirements in Regulating the Water and Solute Composition of the Internal Environment

Vertebrates, both mammalian and nonmammalian, survive and, indeed, thrive under a very wide range of environmental conditions. Some live in arid environments in which conservation of water is of great importance. Others live in completely aqueous freshwater environments in which excretion of excess water and retention of important inorganic solutes are essential. Still others live in completely aqueous marine environments. Here, the high osmolality of the surrounding seawater either requires osmotic conformity with the medium or the retention of water and the excretion of excess solutes, including not only sodium and chloride but also large quantities of ingested divalent ions, such as calcium, magnesium, phosphate, and sulfate. Even some of those species that conform to a marine environment, however, must adjust the solute composition of their internal environment. Many species, particularly terrestrial ones, tolerate variations in their solute and water requirements; other species, particularly aquatic ones, even move from one environmental extreme to another, for example, from seawater to freshwater.

1.3 Possible Roles of Kidneys in Regulating Water and Solute Composition of the Internal Environment

As noted above, kidneys generally play a role in regulating the solute and water composition of the internal environment. Some information on this role is available for species from the major vertebrate classes: cyclostomes (Agnatha), both the

myxini (hagfishes) and petromyzones (lampreys); elasmobranchs (Chondrichthyes); bony fishes (Osteichthyes), primarily teleosts, but also lungfish; amphibians (Amphibia), both urodeles and anurans; reptiles (Reptilia), primarily Testudinea, Squamata, and Crocodylia, but also Rhynchocephalia; Birds (Aves); and mammals (Mammalia). However, only among the mammals is the kidney essentially of sole importance in regulating the solute and water composition of the internal environment. Among all other vertebrate groups, extrarenal routes for the regulation of solute and water movements, or postrenal modification of ureteral urine, or both are also important. For example, among the cyclostomes, the role of the kidney in the regulation of solute and water balance appears to be substantially greater in the lampreys than in the hagfish, but in both groups regulation of solute and water movement across the gills and, possibly, the integument or within the gastrointestinal tract may be significant. Renal function is clearly important in solute and water balance in marine elasmobranchs, but a specialized extrarenal route (rectal gland) for sodium chloride excretion also exists and ion and water movements across the gills may be regulated. Among the euryhaline teleosts, the kidneys are particularly important in adaptation of the animals to freshwater or seawater, but regulation of renal function is clearly coordinated with regulation of ion and water movement across the gills. Although renal function is very important in regulating solute and water excretion in amphibians, it is also coordinated with postrenal ion and water movements across the bladder or cloaca and with ion and water movements across the integument. Among reptiles and birds, renal function, although highly significant in regulating the composition of the internal environment, again must be coordinated with the regulation of postrenal transport of ions and water across the bladder, cloaca, or colon and, in some species, with the regulation of ion excretion by extrarenal salt glands. In some reptilian species, there may be regulation of ion and water movements across the integument. Unfortunately, the exact quantitative relationships among the various routes of solute and water excretion have not been delineated for any species of nonmammalian vertebrate. Nevertheless, regulation of renal function must, in some way, be carefully integrated and coordinated with regulation of these other routes of water and solute movement, as well as with the behavior of the animals, in their total adaptation to their environment. These coordinated relationships certainly deserve careful quantitative study.

Even for renal function alone, many variations exist among vertebrates. Present knowledge is insufficient to permit a complete description of these variations or the mechanisms underlying them. Nevertheless, in this volume I attempt to describe and analyze all those renal functions in nonmammalian vertebrates for which there is some information available. For this purpose, I begin with a brief description of both gross and fine structure of the kidneys. I then move to a consideration of the initial process in urine formation, primarily ultrafiltration of the plasma at the renal glomerulus but also secretion of fluid by the renal tubules. I then cover transport of inorganic ions, fluid, and organic substances by the renal tubules and regulation of these transport processes. I consider renal aspects of acid–base balance only in terms of tubular transport. Following these discussions, I cover the processes involved in producing urine hypoosmotic or hyperosmotic to plasma, their relative importance,

and their regulation. Throughout the book, I compare and contrast renal mechanisms among the vertebrates. However, I devote a final chapter (Chap. 8) to an integrated (although, by necessity, somewhat simplified) summary of renal function for each vertebrate group and summary comparisons of several major renal functions for which adequate information is available among vertebrate groups.

1.4 Useful Reviews on Comparative Renal Physiology

The present volume covers all major aspects of vertebrate renal physiology from a comparative viewpoint. Other reviews consider specific renal functions from a comparative viewpoint, renal function in specific animal groups only, or comparative renal function in nonmammalian vertebrates only. Unfortunately, some of these are quite dated. Nevertheless, because a number of these provide excellent coverage of some of these topics, I have provided a selection here. References to many other shorter reviews on specific aspects of renal function are provided throughout the following chapters.

The most recent reviews cover renal function in individual vertebrate classes only. The most recent of these are found in the sections of the chapter “Osmoregulation and Excretion” (Larsen et al. 2014) in *Comprehensive Physiology* (online: comprehensivephysiology.com). Another series of recent chapters covering renal function in individual vertebrate classes are found in the volume *Osmotic and Ionic Regulation: Cells and Animals* (Evans 2009).

All other reviews are much older. The most recent of these on integrative physiology of the vertebrate kidney is the chapter “Vertebrate Renal System” (Braun and Dantzler 1997) in *Handbook of Physiology. Comparative Physiology* (now online: comprehensivephysiology.com). Other similar reviews were written close to the same time as the first edition of this book. These include the chapters “Comparative Aspects of Renal Function” (Dantzler 1992a) in *The Kidney: Physiology and Pathophysiology*, 2nd edition and “Comparative Physiology of the Kidney” (Dantzler 1992b) in *Handbook of Physiology. Renal Physiology* (now online: comprehensivephysiology.com).

Finally, a series of even older review chapters or monographs are available on single major groups of vertebrates. These include reviews on fishes (Hickman and Trump 1969), reptiles (Dantzler 1976) and birds (Skadhauge 1973, 1981).

References

- Braun EJ, Dantzler WH (1997) Vertebrate renal system. In: Dantzler WH (ed) *Handbook of physiology: Comparative physiology*. Oxford University Press, New York, pp 481–576
- Dantzler WH (1976) Renal function (with special emphasis on nitrogen excretion). In: Gans CG, Dawson WR (eds) *Biology of Reptilia*, vol 5, *Physiology A*. Academic Press, London, pp 447–503

- Dantzler WH (1992a) Comparative aspects of renal function. In: Seldin DW, Giebisch G (eds) *The kidney: Physiology and pathophysiology*, 2nd edn. Raven, New York, pp 885–942
- Dantzler WH (1992b) Comparative physiology of the kidney. In: Windhager EE (ed) *Handbook of physiology-renal physiology*. Oxford Press, New York, pp 415–474
- Evans DH (ed) (2009) *Osmotic and ionic regulation. Cells and animals*. CRC Press, Boca Raton, FL
- Hickman CP Jr, Trump BF (1969) The kidney. In: Hoar WS, Randall DJ (eds) *Fish physiology*, vol I, Excretion, ion regulation, and metabolism. Academic, New York, pp 91–239
- Krogh A (1929) The progress of physiology. *Am J Physiol* 90:243–251
- Larsen EH, Deaton LE, Onken H, O'Donnell M, Grosell M, Dantzler WH, Weihrauch D (eds) (2014) Osmoregulation and excretion. *Compr Physiol* 4:405–573
- Skadhauge E (1973) Renal and cloacal salt and water transport in the fowl (*Gallus domesticus*). *Dan Med Bull* 20:1–82
- Skadhauge E (1981) *Osmoregulation in Birds*. Springer, Berlin

Chapter 2

Renal Morphology

Abstract This chapter first covers the gross internal and external renal morphology of fishes, amphibians, reptiles, birds, and mammals. This discussion begins by considering the segments of the prototypical vertebrate nephron. It then examines the variations in nephron segments from this prototype and the arrangement of the nephrons within the kidney in each vertebrate class. In particular, it emphasizes certain specific variations in gross nephron structure such as the aglomerular nephrons in some fishes and a few reptiles, the extremely complex nephrons of elasmobranch fishes, and the presence and arrangement of reptilian-type (loopless) and mammalian-type (looped) nephrons in birds. The discussion of gross morphology also includes a brief consideration of the blood vessels, emphasizing the variation in the complexity of glomerular capillaries in different vertebrate classes and the presence of a renal venous portal system in the kidneys of all amphibians, reptiles, birds, marine teleost fishes, and probably euryhaline teleost fishes. The chapter then briefly explores the fine structure of the glomerulus, especially the filtration barrier, and of the nephron segments found in each vertebrate class. It ends with a short discussion of the juxtaglomerular apparatus found in mammals and portions of it found in nonmammalian vertebrate species.

Keywords Comparative renal morphology • Gross structure • Fine structure • External morphology • Internal morphology • Glomerulus structure • Tubule structure • Vasculature structure

2.1 Introduction

Similarities and differences exist among vertebrate classes in gross external morphology, internal organization, and cellular structure of the kidneys. Since these similarities and differences are related to similarities and differences in renal function, some knowledge of structure is required for understanding function. However, this volume is not a treatise on renal morphology and only those known morphological features that appear most important for an understanding of comparative renal function are discussed in this chapter. Some additional structural details, not covered here, are discussed in the context of function in later chapters.

2.2 Gross External and Internal Morphology

2.2.1 General Considerations

The prototypical vertebrate nephron consists of a glomerulus followed by a neck segment, a proximal tubule, an intermediate segment, a distal tubule, and, finally, a collecting tubule and duct system (Figs. 2.1 and 2.2). However, variations in the occurrence and structure of these specific nephron components (Fig. 2.2), in the relationship of different nephron segments to their blood supply and to each other, and in the relationship of individual nephrons to each other are found within and between vertebrate classes. These relationships also help to define the gross external morphology of the kidney. The most significant variations in these structures and their relationships are considered below and later will be considered in more detail in relation to function.

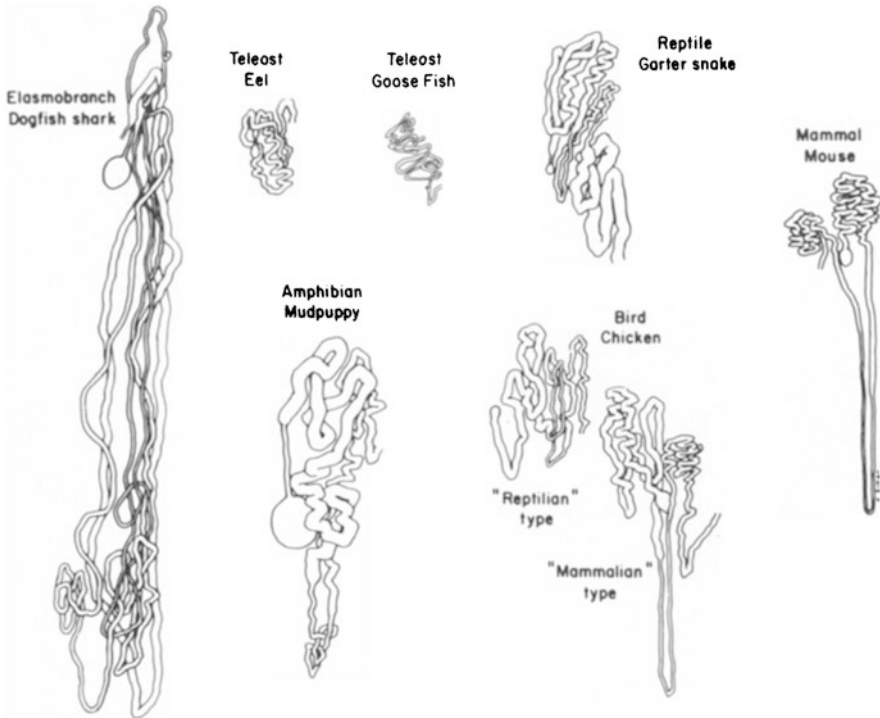


Fig. 2.1 Representations of fish (elasmobranch, *Squalus acanthias*; glomerular teleost, *Anguilla rostrata*; aglomerular teleost, *Lophius piscatorius*), amphibian (*Necturus maculosus*), reptilian (*Thamnophis sirtalis*), avian (domestic fowl, *Gallus gallus*), and mammalian (*Mus flavicolis*) nephrons drawn to a single scale (After Long and Giebisch 1979; Marshall and Grafflin 1928; reproduced from Dantzler 1992, with permission)

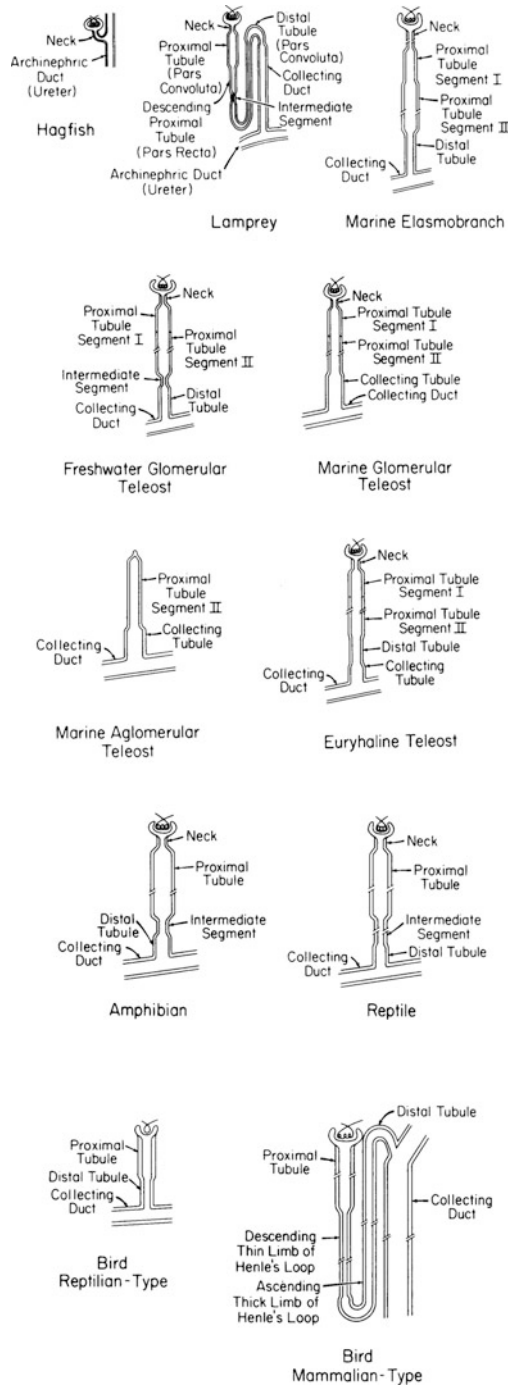


Fig. 2.2 Diagrammatic representations of nephrons from the major classes of nonmammalian vertebrates to show the major nephron segments. No attempt was made to draw nephrons to an exact scale, although some attempt was made to indicate relative sizes for fish and bird nephrons.

2.2.2 Fishes

2.2.2.1 Cyclostomes

Among the cyclostomes, the adult Myxini (hagfishes), which conform to their marine environment, at least in terms of the osmolality of their body fluids, retain paired apparently nonfunctional pronephric kidneys as well as paired functional mesonephric kidneys. Each of the paired mesonephric kidneys contains 30–35 very large, oval glomeruli arranged segmentally on the medial side of a primitive archinephric duct (ureter) (Fig. 2.2). Each glomerulus is connected to the archinephric duct by a short, non-ciliated neck segment (Fig. 2.2) (Fels et al. 1998; Hickman and Trump 1969). There are no other nephron segments.

The adult Petromyzones (lampreys), which apparently do not conform to their environment, thus maintaining body fluids hypoosmotic to a marine environment and hyperosmotic to a freshwater environment, have nephrons similar in gross structure to more advanced vertebrates (Hickman and Trump 1969; Logan et al. 1980). Each has a glomerulus, a ciliated neck segment, a proximal tubule, an intermediate segment, a distal tubule, and a collecting duct (Fig. 2.2). Although early studies suggested that the urinary space of adjacent glomeruli might be continuous in some species (Regaud and Policard 1902; Youson 1975), the most recent studies indicate that this is not so (Logan et al. 1980). Each nephron apparently has a major loop segment arranged parallel to its own collecting duct (Fig. 2.2) (Logan et al. 1980), but the functional significance of this loop is unknown. The nephrons do not appear to be arranged in a manner that permits them to function in concert to produce urine hyperosmotic to the plasma (vide infra; Chap. 7). In the sea lamprey, *Petromyzon marinus*, the entire loop consists of distal tubule (Youson and McMillan 1970a), whereas in the river lamprey, *Lampetra fluviatilis*, the descending limb of the loop consists of proximal tubule and the ascending limb of distal tubule (Fig. 2.2) (Morris 1972).

2.2.2.2 Stenohaline Marine Elasmobranchs

Marine elasmobranchs, like hagfishes, conform to the osmolality of their environment, but, unlike hagfishes, much of the osmolality of the extracellular fluid is determined by the concentrations of urea and trimethylamine oxide (TMAO). Nephrons in these animals contain all the standard vertebrate components noted above (Figs. 2.1 and 2.2) (Hickman and Trump 1969), but the arrangement of the

Fig. 2.2 (continued) Breaks in the nephrons indicate that the lengths of those segments may be much greater, relative to other segments, than actually shown. Except for those nephrons in which a loop structure was parallel to the collecting ducts (lamprey and avian mammalian-type), no attempt was made to show the shape of the nephron segments (Dantzler 1992, with permission)

nephrons is highly complex, arguably the most complex of any vertebrate kidney. Although the elasmobranch kidney is not organized into discrete cortical and medullary regions like the mammalian kidney, the nephrons are arranged to permit countercurrent flow within the dorsolateral region of the kidney (see Fig. 2.3, and its legend for a detailed description of this arrangement) (Boylan 1972; Deetjen and Antkowiak 1970; Evans and Claiborne 2009; Lacy et al. 1975). Moreover, the five nephron segments so arranged and the peritubular capillaries arranged in countercurrent fashion among them are encapsulated in a peritubular sheath (Fig. 2.3), which may serve to create a microenvironment in which some form of countercurrent exchange or, possibly, countercurrent multiplication can operate. Such a process may be very important in the retention of urea by the kidneys of marine elasmobranchs (vide infra; Chap. 6).

2.2.2.3 Euryhaline and Stenohaline Freshwater Elasmobranchs

Euryhaline elasmobranchs when in freshwater and stenohaline freshwater elasmobranchs maintain their extracellular osmolality above that of freshwater but reduce it below that of seawater, primarily by reducing the urea concentration (Evans and Claiborne 2009). The nephron structure and arrangement appear to vary depending on whether the species is a euryhaline one or a stenohaline freshwater one. For example, the euryhaline Atlantic stingray (*Dasyatis Sabina*) has a renal structure essentially the same as that described above for marine elasmobranchs (Fig. 2.3) (Lacy and Reale 1999). However, the kidney of the stenohaline freshwater stingray (*Potamotrygon* sp.) has the dorsolateral bundle zone (described in Fig. 2.3) replaced by a peripheral complex zone containing the glomeruli and lacking the peritubular sheath surrounding the tubule segments (Lacy and Reale 1999). The ventromedial sinus zone (described in Fig. 2.3) is replaced with a central sinus zone (Lacy and Reale 1999). The *Potamotrygon* kidney also lacks loops III and IV of the tubules shown for the marine elasmobranch kidney in Fig. 2.3 (Lacy and Reale 1999). It is assumed that the kidneys of other stenohaline freshwater species would also have this modified structure and that the absence of nephron loops III and IV is related to the inability of the nephrons in these species to reabsorb filtered urea (vide infra; Chap. 6), but there are no physiological studies on this possible function.

2.2.2.4 Stenohaline Marine Teleosts

Stenohaline marine teleosts maintain the osmolality of their body fluids well below that of their environment. Grossly, their kidneys are divided into an anterior head kidney containing lymphoid, hematopoietic, and glandular tissue and a posterior trunk kidney containing the renal tissue, but in many species the two kidneys are partially or completely fused and cannot be distinguished by external examination (Hickman and Trump 1969). The nephrons of glomerular stenohaline marine

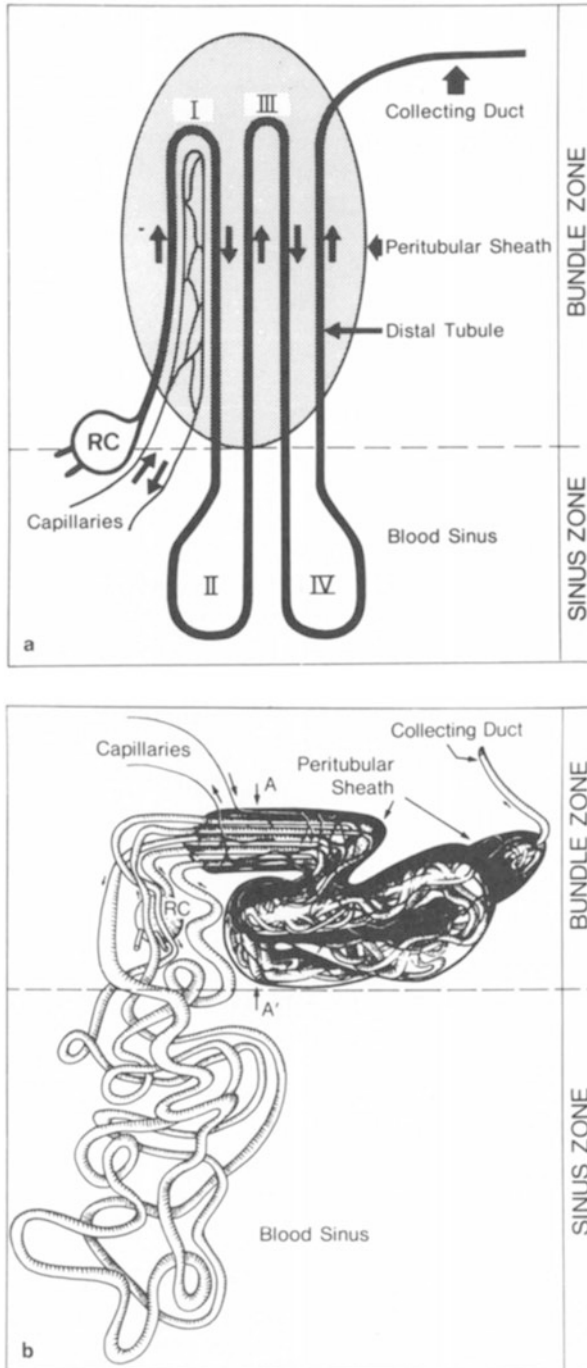


Fig. 2.3 Diagram of elasmobranch nephron in bundle zone (dorsolateral region) and sinus zone (ventromedial region). The dorsal surface is parallel to the top of the page. (*Part a*) Simplified diagram showing renal corpuscle (RC) (Glomerulus) and four highly stylized nephron loops (I–IV).

teleosts generally contain, in addition to a glomerulus, a neck segment, two or three proximal segments that constitute the major portion of the nephron, sometimes an intermediate segment between the first and second proximal segments, and a collecting tubule emptying into the collecting duct system (Fig. 2.2).

As would be expected in marine animals that do not have to dilute the urine to excrete excess water (vide infra; Chap. 7), the distal tubule is absent in almost all species (Hickman and Trump 1969) and, where present, may actually indicate some degree of euryhalinity. Although the entire proximal tubule has a brush border, only the first segment is ultrastructurally similar to the proximal convoluted tubule of mammals (Hickman and Trump 1969).

As would also be appropriate for marine fish that need to minimize their urine volume, some thirty species have nephrons lacking a glomerulus (Fig. 2.2) (Evans and Claiborne 2009; Hickman and Trump 1969). These aglomerular nephrons typically have only a single proximal segment with a brush border similar to that of the second proximal segment of the nephrons of glomerular teleosts and a collecting tubule (Fig. 2.2).

2.2.2.5 Stenohaline Freshwater Teleosts

Stenohaline freshwater teleosts, which maintain the osmolality of their body fluids well above that of their environment, have nephrons that differ from those of stenohaline marine teleosts. Grossly, the head and trunk kidneys are fused to a large extent (Hickman and Trump 1969). The nephrons of glomerular species typically contain, in addition to a glomerulus, a ciliated neck segment, an initial proximal segment with a prominent brush border, a second proximal segment with

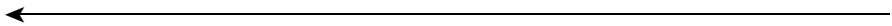


Fig. 2.3 (continued) A peritubular sheath surrounds the countercurrent system of nephron segments (loops I, III, and the distal tubule) and anastomosing capillary loops in the bundle zone (gray color shows area enclosed by peritubular sheath). *Small arrows* indicate the direction of tubular fluid and blood flow. (*Part b*) Schematic drawing of the pathway of the skate nephron in the bundle zone (dorsolateral region) and in the sinus zone (ventromedial region) showing some of the nephron complexity. As shown diagrammatically in *Part a*, the entering limbs of nephron loops I and III and the distal tubule pierce the peritubular sheath near the renal corpuscle and extend to the opposite end of the sheath. Close to the renal corpuscle, the five tubule segments (loops I, III, and the distal tubule) located in the bundle zone are covered by the peritubular sheath and run parallel to each other (to emphasize this distinctive course, they have been drawn side by side in one plane and not assembled into a bundle as they actually are). The tubule bundle and surrounding peritubular sheath then become convoluted, and the parallel course of the tubules is lost as the loops wrap around each other (shown schematically in *Part b*). For simplicity, the opposite end of the peritubular sheath, where the distal tubule emerges, has been drawn away from the renal corpuscle on the far right side of the diagram and the schematic. The distal tubule pierces the sheath at this point to join the collecting duct, whereas the other two nephron segments loop back and retrace their path, finally exiting the sheath where they entered it. Capillaries also enter and exit the peritubular sheath at its renal corpuscle terminus and form an anastomotic network around and within the bundle (Lacy et al. 1985, with permission)

a less prominent brush border, an intermediate segment, and a distal tubule emptying into the collecting duct system (Fig. 2.2). The kidneys of most stenohaline freshwater teleosts, as might be expected in animals that need to excrete much water, tend to have more nephrons with larger glomeruli than those of stenohaline marine teleosts. Interestingly, the glomeruli of some apparently stenohaline freshwater teleosts that survive adaptation to seawater atrophy and disappear (Elger and Hentschel 1981). The few aglomerular freshwater teleosts (apparently species that evolved in seawater and later invaded freshwater) seem to have nephrons entirely like those of marine aglomerular species (Fig. 2.2) (Hickman and Trump 1969).

2.2.2.6 Euryhaline Teleosts

These animals, which can maintain the osmolality of their body fluids above that of the environment when adapted to freshwater and below that of the environment when adapted to seawater, have nephrons most similar to those of stenohaline freshwater teleosts. These typically have a glomerulus (often smaller and less vascular than in stenohaline freshwater species), a first proximal segment, a second proximal segment, a variably present short intermediate segment, a distal tubule, and a collecting tubule emptying into the collecting duct system (Fig. 2.2) (Hickman and Trump 1969). Interestingly, some euryhaline species are actually aglomerular (e.g., the toadfish, *Opsanus tau*) (Baustian et al. 1997; Lahlou et al. 1969). Moreover, in glomerular euryhaline species, the number of glomeruli filtering can vary from sea water to freshwater (Brown et al. 1980) (vide infra; Chap. 2).

2.2.3 Amphibians

The external shape of the mesonephric kidneys of amphibians, whose habitats range from completely aqueous to arid terrestrial, varies substantially among species. They tend to be elongated with some evidence of segmentation in urodeles and relatively short and compact in anurans. However, basic internal renal organization is rather similar for all amphibians and can be illustrated by that of the frog kidney shown in Fig. 2.4. All nephrons contain a glomerulus, ciliated neck segment, proximal tubule, ciliated intermediate segment, and distal tubule emptying into the collecting duct system (Figs. 2.1, 2.2, and 2.4) (vide infra; Sect. 2.3 for cellular segmental subdivisions). Of particular note, as in most other nonmammalian vertebrates, the nephrons empty at right angles into the collecting ducts. There are no discrete cortical and medullary regions and no lengthened intermediate nephron segments arranged parallel to collecting ducts as in avian and mammalian kidneys (2.4).

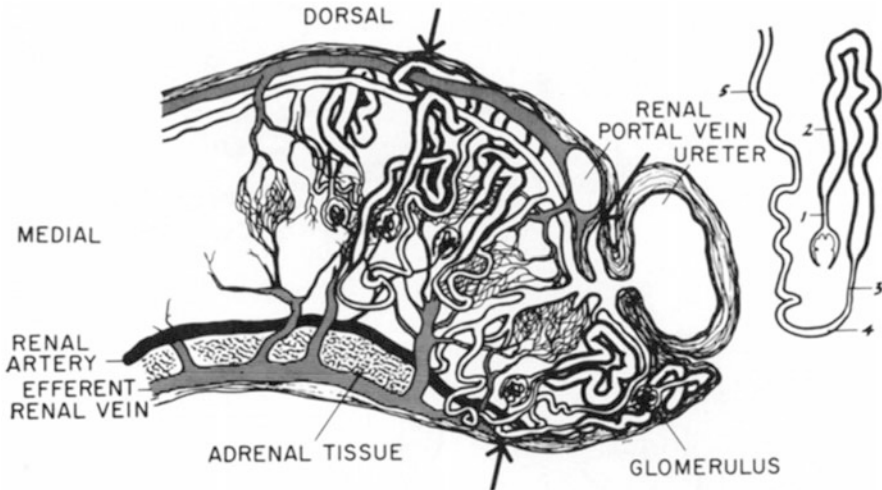


Fig. 2.4 Cross-section of frog kidney, adapted from von Mollendorf (1930). 1 neck segment; 2 proximal tubule; 3 intermediate segment; 4 distal tubule; 5 collecting duct. Arrows designate typical micropuncture sites (Long 1973, with permission)

2.2.4 Reptiles

Like the mesonephric kidneys of adult amphibians, the metanephric kidneys of adult reptiles, whose habitats also range from completely aqueous to arid terrestrial, show marked variation in their external morphology. This is undoubtedly due to the extreme variation in body form within the class Reptilia, as exemplified by the ophidians on one hand and chelonians on the other. As examples, the kidneys of saurians are compact, somewhat triangular-shaped structures joined at the posterior end, those of ophidians are long and thin, and those of chelonians are constrained by the shape of the carapace (Dantzler and Bradshaw 2009) (Dantzler, personal observations). These varying kidney shapes also determine the gross arrangement of the nephrons. For example, ophidian nephrons lie side by side in neat parallel rows and attach at roughly right angles to major collecting ducts (Fig. 2.5) (Dantzler, personal observations), whereas saurian nephrons branch off the collecting ducts more obliquely and are arranged in compact bunches (O'Shea et al. 1993). Again, however, although the external shape of the kidneys varies among the Reptilia, the internal organization of these organs is reasonably uniform. This basic organization is illustrated diagrammatically for the snake kidney in Fig. 2.5. The nephrons are generally composed of all standard components—glomerulus, ciliated neck segment, proximal tubule, ciliated intermediate segment, and distal tubule (Fig. 2.2)—and they empty at right angles into collecting ducts (Fig. 2.5). However, a few nephrons without glomeruli have been described in some ophidians (Regaud and Policard 1903) and in one saurian species (O'Shea et al. 1993). Again, as in amphibian kidneys, in reptilian kidneys there are no