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PREFACE

Readers of the *Annual Review of Physiology* are familiar with each volume's format that presents recurring, if not always traditional, sections that are thematic in organization. The themes in each section change yearly in response to the Editorial Committee's perception of current advances and the stage of maturation of the various areas comprising the subject matter of physiology. Because developments are rapidly occurring outside the traditional fields of physiology, the Editorial Committee also includes special topics, the purpose of which is to bring to the attention of our readers areas of related interest and usefulness. The special topics covered in this volume are Physiological Aspects of Nuclear Magnetic Resonance and Chemosensory Transduction. In addition there is an interdisciplinary theme of Signal Transduction, the specifics and generalities of which cross the customary alignments.

In order to function optimally and responsibly the Editorial Committee needs and seeks input from our colleagues and encourages the submission of suggestions to any of its members. We are aware of divergent as well as convergent aspects of the changing scene of physiological science that includes, on the one hand, cellular and molecular developments and, on the other, systems and whole animal integrations. We are also aware that much of the excitement of current work embodies the study of interrelationships among these various levels. So the pendulum of insight and understanding in constant motion across these diverse approaches will continue to yield new syntheses of physiological processes that the Committee hopes are duly recounted in our series volumes.

Joseph F. Hoffman
Editor

OTHER REVIEWS OF INTEREST TO PHYSIOLOGISTS

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From the *Annual Review of Pharmacology and Toxicology*, Volume 32 (1992):

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Biochemical and Molecular Pharmacology of Kinin Receptors, S. G. Farmer and R. M. Burch
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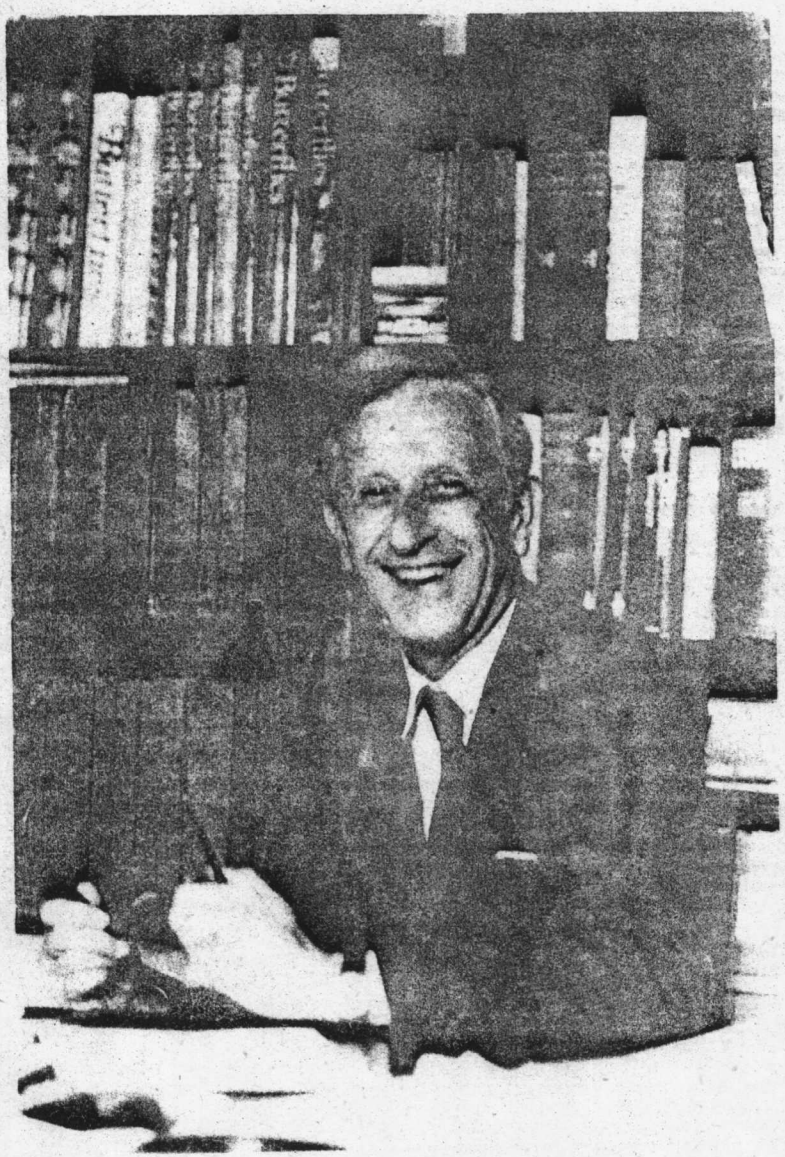

François Morel

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METHODS IN KIDNEY PHYSIOLOGY: PAST, PRESENT, AND FUTURE

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KEY WORDS: kidney tubules, microperfusion, microtechniques

INTRODUCTION

In the letter inviting me to prepare this prefatory chapter, the Editor of Annual Review of Physiology indicated that the author is now expected to "summarize the key background material, provide a state-of-the-art view of the subject, pose the important unanswered questions (as well as approaches to possible solutions) and speculate a bit about future developments."

I entered the field of kidney physiology about forty years ago, namely, when this domain of physiology was expanding quite rapidly. Since that time, I have enjoyed observing how experimental sciences progress and why, sometimes, a break-through changes their course. In fact, the history of kidney physiology illustrates perfectly how often new steps in physiology required the development of appropriate methods so designed as to answer right questions. I hope to keep in line with the Editor's advice when devoting this prefatory chapter to the relationships between progress in methods and knowledge in the past, present, and future of kidney physiology.

PAST

Although the key role of kidneys in body fluid homeostasis has been well-recognized for a long time, and the intricate anatomical organization of

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nephrons has been established, advances in renal physiology were initiated following the introduction of two specific techniques: (*a*) Firstly, the in vivo micropuncture of tubular fluid from amphibian kidneys, introduced by Richards and associates (16, 17, 22), made it possible to demonstrate the relevance of the filtration-reabsorption theory of kidney function and to analyze changes in tubular fluid composition that occur along successive nephron portions. At that time, however, micropuncture experiments, which required microanalyses with less than one microliter samples of fluid, were tedious and few physiologists performed them. (*b*) Secondly, the discovery by Homer Smith that inulin represents an ideal marker for measuring the glomerular filtration rate (GFR) led to the development of the renal clearance technique (18): GFR measurements with inulin made it possible to calculate accurately overall rates of tubular transport (reabsorption or secretion) for any kind of filtered molecular species simply by measuring the concentrations of inulin and of the studied species in collected urine and blood plasma samples. The clearance technique could be used to study quantitatively a great variety of questions related to kidney functions under normal, experimental, or physiopathological conditions in laboratory animals and in humans. As a consequence, use of this new approach spread rapidly and resulted in the tremendous development of kidney physiology, which occurred after World War II. It should be pointed out, nevertheless, that clearance data, although accurate, correspond only to a balance measurement between filtered load (input) and urinary excretion rate (output): the kidney itself remains a black box. In particular, clearance measurements give no information about the nephron segments where the observed net solute transport take place. This limitation could be overcome by extrapolating to the mammalian kidney the precise localizations previously established for the same solutes by micropuncture in the amphibian kidney. Our present basic knowledge of main kidney functions has been largely acquired in this way.

However, extrapolation to mammals of amphibian micropuncture data later proved to be completely inadequate to explain the mechanism of urine concentration. It is now clear that this failure originated in the fact that the amphibian kidney has no loops of Henle and is unable to produce hypertonic urine. At that time, it appeared necessary that water must be actively reabsorbed (out of late distal tubules and perhaps collecting tubules) in order to account for the formation by the mammalian kidney of urine hyperosmotic to plasma (vasopressin-dependent "facultative water reabsorption") (19). Although erroneous, this view appeared so coherent and was so widely accepted that eight years elapsed before the mechanism of urine concentration in collecting tubules by passive water abstraction along a medullary gradient of osmotic pressure, as proposed by Wirz et al as early as 1950 (24), was finally accepted and the role of Henle's loops was recognized in 1959 (20).