Peritoneal Dialysis

New Concepts and Applications

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Dedicated to peritoneal dialysis patients

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Foreword

The tremendous changes that have occurred in peritoneal dialysis in the last 25 years have transformed the technique from a second-class therapy (compared with hemodialysis) to a measure that is the equal of hemodialysis in many respects and even superior to hemodialysis in terms of cost, maintenance of hemoglobin, and independent living.

The revolution began with the introduction of continuous ambulatory peritoneal dialysis (CAPD) by Popovich and Moncrief, who deserve the lion's share of credit for our progress. The introduction of plastic bags and the Toronto Western Hospital technique for CAPD led to the widespread acceptance of this mode of dialysis and to a significant reduction in the frequency of peritonitis from one episode every 3 to 4 patient months to one episode per patient year. In the last few years peritonitis rates fell further after the introduction of the Y-set system by Buoncristiani. Today many centers achieve peritonitis rates of less than one episode per 2 patient years.

The editors of this volume, Twardowski, Nolph, and Khanna, have made important contributions to our knowledge of the physiology of peritoneal dialysis as well as to its various clinical aspects.

Automated peritoneal dialysis, in the form of either continuous cyclic peritoneal dialysis (CCPD), which was proposed and advanced by Suki and Diaz-Buxo, or the more expensive nightly intermittent peritoneal dialysis, (IPD) is gaining ground; thus, we are able to maintain a number of patients who cannot be managed by CAPD and otherwise would be converted to hemodialysis.

CAPD plays a particularly important role in the management of children and diabetics with end-stage renal disease. Maiorca describes the experience of his group in the Y-system chapter, illustrating what CAPD can achieve in adults.

The last few years have witnessed great advances in our understanding of the anatomy and physiology of the peritoneal membrane, the complex function of the mesothelial cells, and the role of lymphatics during peritoneal dialysis. However, despite these advances, major problems remain; all who wield influence should encourage the continued dedication of the pioneers as well as the work of new scientists in the field. We need financial support for scientists from many disciplines, who will contribute their ingenuity to solving the lingering problems. These challenges include prevention of exit-site infection and subsequent peritonitis; malnutrition; and ultrafiltration failure. Of course, all who have worked with CAPD over the years are

conscious of the risk of encapsulating sclerosing peritonitis—the precise mechanisms of which have yet to be identified.

Although a significant number of patients have remained on CAPD for 10 years or more, it has not yet been established that CAPD is a true long-term dialysis modality.

Our progress to date gives me the encouragement to believe that we will solve most of the problems and that CAPD will take its place among the genuine kidney-replacement techniques, thus providing the nephrologist with a wide range of alternatives in the management of patients with end-stage renal disease.

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Preface

One cannot know everything.
Horace

Treatment of uremia by intraperitoneal infusion and drainage of dialysis solution was first reported in 1923 by Georg Ganter, a German physician. Ganter found followers very quickly, and in the next 25 years, more than 100 cases of such treatment were reported. The development of the Tenckhoff catheter in 1968 and, particularly, the introduction of continuous ambulatory peritoneal dialysis (CAPD) in the late 1970s encouraged the use of peritoneal dialysis in the treatment of chronic renal failure. The development of new catheters, automated cycling equipment, variable flow techniques, and many other techniques have yielded both improved results and increased interest in peritoneal dialysis; by the end of 1989 more than 45,000 patients worldwide were on peritoneal dialysis.

Research is intense, with more than 400 papers related to peritoneal dialysis published annually. With such rapid progress, a book devoted to the latest developments in the field cannot be written by a few persons; it must be a multiauthored volume. The authors have written up-to-date, comprehensive, extensively referenced chapters. We have selected for discussion in this volume areas of peritoneal dialysis we believe to be most important and that have been central to the most striking recent progress in the field.

Many contributors have been our colleagues in the Department of Medicine at the University of Missouri; we have followed the work of the other authors for many years, and are pleased to have their contributions. Lazaro Gotloib and Avshalom Shostak, leading students of peritoneal anatomy, have written an excellent chapter on the functional anatomy of the peritoneum as a dialyzing membrane, describing new discoveries relative to fenestrated capillaries, lymph drainage, and the structural basis of transperitoneal transport. Rosario Maiorca and Giovanni C. Cancarini have contributed the chapter on the Y-set, the system that revolutionized peritoneal dialysis connectology and dramatically reduced the rate of peritonitis, the scourge of peritoneal dialysis. Our Italian colleagues have long reported excellent results with this system; now their methods are emulated in other countries. James A. Delmez, a most erudite scholar in the field of bone metabolism and peritoneal dialysis, has authored the chapter on bone and mineral metabolism in CAPD patients. His topics include recent advances in the use of calcium carbonate as a phosphate binder, prevention of hypercalcemia with low calcium dialysis solution, and aluminum toxicity and its treatment. Steven R. Alexander, one of the pioneers of peritoneal dialysis in

children, has coauthored the chapter on CAPD and continuous cyclic peritoneal dialysis results in the United States pediatric population.

E. Dale Everett, Director of the Division of Infectious Diseases in our department, who has been helping us treat infectious complications since the beginning of our CAPD program in 1977, has written a chapter on prevention, diagnosis, and treatment of peritonitis. Robert Mactier has authored the chapter on kinetics of ultrafiltration, a topic he studied during his fellowship in our department. In addition, Sunder Lal, a current member of our faculty and our former fellow, has coauthored a chapter on pharmacologic manipulations of peritoneal transport.

Finally, we have prepared chapters in areas of our own research involvement: adequacy of dialysis and newer cycler techniques; peritoneal access; clinical results with peritoneal dialysis according to experiences of four registries in three continents; and peritoneal dialysis in diabetics.

We thank the chapter authors for timely delivery of the manuscripts, allowing the book to be published on schedule. We are proud to have the contribution of Dimitrios G. Oreopoulos, a pioneer of peritoneal dialysis and editor of *Peritoneal Dialysis International*, who has written the foreword. We also thank Jan Leroux for indispensable secretarial assistance. Finally, we wish to acknowledge the invaluable help of the Churchill Livingstone staff, particularly Linda Panzarella, Avé McCracken, and Marian Ryan, without whose technical assistance publication of the book would not have been possible.

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The Functional Anatomy of the Peritoneum As a Dialyzing Membrane

Lazaro Gotloib
Avshalom Shostak

There is not one science of chemistry, another of electricity, another of medicine and so on. There is only one natural world and there is only one knowledge of it.
Sir William Bragg, 1941

INTRODUCTION

The beginning of the 16th century saw the dawn of the peritoneal function as interpreted by Asellius (1581–1626) in the mesentery of dogs.

Since that time, morphologic,[1–4] physiologic,[5–8] and clinical studies[9–13] have given strength and scientific foundation to the idea of using the peritoneum as a dialyzing membrane for long-term care of chronic uremic patients. However, four centuries of intensive, multidisciplinary research failed to completely disclose the way in which nature has solved the blood-tissue contact problem. A rational, analytic approach to the problems of peritoneal

permeability should be based on the morphologic and functional analysis of each of the several components of the peritoneal dialysis system.[8] Consequently, in this review the peritoneal membrane is conceived as the embodiment of several biologic membranes, each showing more or less specific morphologic and even molecular characteristics. Our main goal is to merge the available morphologic and physiologic information, as well as to define the chief unanswered questions that should eventually be solved by future research.

BLOOD MICROVESSELS

Blood microvessel capillaries of the human and rodent parietal and visceral peritoneum have been classically reported to be the continuous type[14] (Fig. 1-1). However, the existence of fenestrated capillaries in the human parietal and rabbit diaphragmatic peritoneum,[15] as well as in the mesentery of mice,[16] has been reported (Fig. 1-2). The incidence of fenestrated capillaries in human parietal peritoneum appears to be low (1.7 percent of the total number of capillaries).[15] However, the presence of fenestrated capillaries in the mesentery, which contributes up to 49 percent of the total mesothelial dialyzing surface area in humans,[17] may be physiologically significant. Furthermore, it should be noted that the density distribution of submesothelial microvessels along the different portions of the peritoneum is heterogeneous. In rabbits, the mesentery appears as the most vascularized peritoneal segment, contributing 71.1 percent of the total number of observed capillaries. Reported diaphragmatic and parietal contributions to the total microvascular bed examined are 17.9 and 10.9 percent, respectively.[18]

The endothelial luminal surface-blood interface, which constitutes the first obstacle for solutes on the way to the peritoneal dialysate, is composed of the stagnant fluid film in the capillary lumen (the functional significance of which has been considered to be minor[8]) and the endothelial cell glycocalix. The latter, originally described by Luft[19] in other vascular beds, has also been observed on the surface of most cells[20] and at the luminal aspect of endothelial cells of peritoneal microvessels.[21-23]

The endothelial cell glycocalix is a regular, well-organized polymeric carpet, the major structural components of which are sialoconjugates, proteoglycans, and acidic polymers, which provide a fibrous network and impart an electronegative charge to the cell luminal membrane (Fig. 1-1, inset).[24-28] This polyanionic coat furnishes a nonthrombogenic surface[29] and contributes to the regulation of the transport of small and large molecules across the vascular wall, acting as a size, shape, and charge barrier.[27,28]

Therefore, the glycocalix can act as a physiologic barrier for anionic plasma proteins. In addition serum albumin, which has a net negative charge, can also bind anions as a result of the presence of cationic groups.[29,30] In this way, in the fiber matrix model of capillary permeability, the glycocalix is viewed as a meshwork of glycoprotein fibers which, by trapping circu-