Vitamin E-Bonded Membrane. A Further Step in Dialysis Optimization
Vitamin E-Bonded Membrane
A Further Step in Dialysis Optimization

Volume Editors
C. Ronco, Vicenza
G. La Greca, Vicenza

101 figures, 2 in color, and 39 tables, 1999
## Contents

<table>
<thead>
<tr>
<th>Page</th>
<th>Title</th>
<th>Authors</th>
</tr>
</thead>
<tbody>
<tr>
<td>IX</td>
<td>Preface</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Introduction</td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>Pathophysiology of the Oxidative Stress and Its Implication in Uremia and Dialysis</td>
<td>Galli, F.; Canestrari, F. (Urbino); Bellomo, G. (Novara)</td>
</tr>
<tr>
<td>32</td>
<td>Vitamin E as an Antioxidant Agent</td>
<td>Taccone-Gallucci, M.; Lubrano, R.; Meloni, C. (Rome)</td>
</tr>
<tr>
<td>44</td>
<td>Chronic Haemolysis and Erythrocyte Survival in Haemodialysis Patients Treated with Vitamin E-Modified Dialysis Filters</td>
<td>Taccone-Gallucci, M. (Rome); Meloni, C. (L'Aquila); Lubrano, R.; Morosetti, M.; Palombo, G.; Cianciulli, P.; Scoppi, P.; Castello, M.A.; Casciani, C.U. (Rome)</td>
</tr>
<tr>
<td>49</td>
<td>Development of Vitamin E-Modified Membrane</td>
<td>Sasaki, M.; Hosoya, N.; Saruhashi, M. (Kanagawa)</td>
</tr>
<tr>
<td>79</td>
<td>Hydraulic and Flow Dynamic Characteristics of Vitamin E-Bonded Dialyzers</td>
<td>Brendolan, A.; Ronco, C. (Vicenza); Ghezzi, P.M. (Cuneo); La Greca, G. (Vicenza)</td>
</tr>
<tr>
<td>89</td>
<td>Urea Clearance and Ionic Dialysance of Excebrane Hemodialyzers</td>
<td>Locatelli, F.; Di Filippo, S.; Manzoni, C. (Lecco)</td>
</tr>
</tbody>
</table>
96 Effect of Several Cellulosic Dialytic Membranes on Hyperhomocysteinemia and on the Oxidative Stress in Dialysis Patients: Any Role for Curay + Vitamin E?

113 Hollow-Fiber Dialyzer Employing Vitamin E-Bonded Membrane: A Morphological Analysis
Ballestri, M.; Tonelli, M.; Inguggiato, P.; Albertazzi, A. (Modena)

128 Does Vitamin E Bound on Dialysis Membrane Improve the LDL Susceptibility to Oxidation? Lessons from an in vitro Model
Morena, M.; Cristol, J.P.; Descomps, B.; Canaud, B. (Montpellier)

139 Effect of Vitamin E Conjugated to Dialysis Membranes on Immunohematopoietic Cell Growth and Signalling
Amato, M.; Aterini, S. (Prato); Pacini, S.; Ruggiero, M. (Firenze)

147 Effects of a Vitamin E-Modified Dialyzer (Excebrane®) on Beta-2-Microglobulin Structure and Removal
Brancaccio, D. (Milan); Bellotti, V. (Pavia); Losi, B.; Padovese, P.; Cozzolino, M.; Carpani, P. (Milan); Mangione, P.; Giorgetti, S. (Pavia); Gallieni, M. (Milan)

156 Lipid Peroxidation, Leukocyte Function and Apoptosis in Hemodialysis Patients Treated with Vitamin E-Modified Filters
Galli, F.; Rovidati, S.; Benedetti, S.; Canestrari, F.; Ferraro, B. (Urbino); Floridi, A.; Buoncristiani, U. (Perugia)

172 Morphologic Evaluation of Red Blood Cells Using Vitamin E-Modified Dialysis Filters
Calzavara, P.; De Angelis, S.; Gatto, C.; Dugo, M.; Puggia, R.; Calconi, G. (Treviso)

177 Excebrane®, Hemocompatibility Studies by the Intradialytic Monitoring of Oxygen Saturation
Ghezzi, P.M. (Cuneo); Ronco, C. (Vicenza)

192 Effect of a New Vitamin E-Coated Membrane on Glycoxidation during Hemodialysis
Odetti, P.; Robaudo, C.; Valentini, S.; Gurreri, G.; Garibaldi, S.; Angeletti, S.; Defferrari, G. (Genoa)

200 In vivo Evaluation of Biocompatibility of a New Dialyzer Employing the Vitamin E-Modified Cellulose Membrane 'Excebrane E': Study of Mechanisms Involved in Mononuclear Cell Activation
Pertosa, G.; Grandaliano, G.; Valente, M.; Montinaro, V.; Soccio, M.; Gesualdo, L.; Schena, F.P. (Bari)
208 Increased Red Blood Cell Survival Reduces the Need of Erythropoietin in Hemodialyzed Patients Treated with Exogenous Glutathione and Vitamin E-Modified Membrane
Usberti, M. (Leno); Bufano, G.; Lima, G. (Cremona); Gazzotti, R.M.; Tira, P. (Leno); Gerardi, G.; Di Lorenzo, D. (Brescia)

215 A Chemiluminescence Assay for the Detection of Reactive Oxygen Species Produced by Human Neutrophils: In vitro Comparison of Vitamin E-Modified Multilayer Hemodialysis Filter with a Polysulfone Dialyzer

226 Immunological Biocompatibility Characterization of a Vitamin E-Bonded Membrane

243 Long-Term Effects of Vitamin E-Bonded Dialysis Membrane on Mononuclear Cell Activation, Malondialdehyde Generation and Endothelial Function in ESRD Patients
Schiecke, G.; Gwinner, W.; Radermacher, J.; Bahlmann, J.; Lonnemann, G. (Hannover)

251 Effect of Vitamin E-Modified Regenerative Cellulose Membrane on Neutrophil Superoxide Anion Radical Production and Lipid Peroxidation

261 Suppressive Effects of Vitamin E-Coated Dialysis Membrane on Hemodialysis-Induced Neutrophil Activation
Sanaka, T. (Tokyo); Omata, M. (Saitama); Nishimura, H.; Shinobe, M.; Higuchi, C. (Tokyo)

269 Author Index
271 Subject Index
Preface

The continuous evolution in techniques and biomaterials has led to significant improvements in hemodialysis therapy. In recent years, major concerns have been expressed about long-term derangements in hemodialysis patients and possible clinically relevant blood membrane interactions. From one side it appears evident that filtration processes may not be adequate to remove the complete spectrum of uremic toxins. Therefore, molecules of different origin and nature may accumulate in the long range and chronic effects may become evident after months or years. From another side, the contact between blood and artificial membranes may lead to the activation of the immunosystem of the patient with possible clinically related disorders. The third aspect which has emerged recently, concerns a series of pathologic events deriving from the generation of reactive oxygen species (ROS). The so-called oxidant stress may be further enhanced in hemodialysis patients by the lack of antioxidant agents and by the interactions between the blood and the biomaterials utilized for renal replacement. Preliminary studies employing biocompatible membranes and antioxidant agents such as vitamin E have demonstrated significant improvements in patient organ function and hemopoietic capacity with increased hematocrit and quality of life. An interesting approach has recently been presented by Terumo Corporation, a company which has provided the nephrological community with a new tool to study the effects of vitamin E on hemodialysis patients. Thanks to a new technology, vitamin E has been bound to the inner surface of a hollow-fiber membrane. Thus, patients’ blood is flowing in contact with a layer of antioxidant agent covering the inner surface of the membrane in the hemodialyzer.

The objective of this book has been to collect a series of original contributions made by a group of leading experts in the field. As editors of this book, we must underline the absolute freedom and independence we were given by the company in preparing the outline, in selecting the topics and the authors, and in
ensuring the honest publication of the results, independently on the obtained data.

We open the series of contributions with an overview on the oxidant stress and vitamin E as antioxidant agent. Furthermore, we asked the R&D department of Terumo to prepare a contribution on the technical aspects of such a membrane and the rationale for its clinical application. The following contributions have been oriented to the description of the hydraulics and the permeability characteristics of the membrane. In the main body of the book we included chapters related to the hemocompatibility of the membrane, its effect on erythrocyte morphology and survival, and the impact on white cell and platelet function. The metabolic effects and the antioxidant impact of the vitamin E-coated membrane have also been presented in the last part of the book completing the spectrum of studies carried out at the present time.

As this book will be published, further studies will certainly be undertaken and for this reason we wish to present this book as a starting point for further speculations and research in this field. Just to analyze some of the future aspects to be studied we can mention the possible effects of the vitamin E-coated membrane on protein glycation, the possible interference with the process of oxidation of nucleic acids and transcription of proteins, the possible reduction of erythropoietin requirement in chronic hemodialysis patients and the possible interaction with the gene expression of molecules such as interferon-γ or various cytokines. Finally, we must consider the possibility of binding the vitamin E molecule to other types of dialysis membrane and the use of the present technology to bind other molecules of biological interest. In this way we really should start to consider a change of the traditionally inert hemodialyzer into a newer device with a great potential for biological interactions with the patient.

Now that this major scientific and organizational enterprise is at its end, we must express our sincere appreciation for the great effort made by the authors delivering their manuscripts timely and in good order. We would also like to express our gratitude to Terumo Corporation for supporting the preparation of this book, and last but not least, we must give our thanks to Dr. Anna Saccardo for the kind organizational assistance and to Karger publishers for the prompt and accurate publication of the work, after truly professional assistance.

We hope that this book, as many others in the series Contributions to Nephrology, will serve as a reference tool for professional nephrologists, fellows and internists involved in the care of end-stage renal disease patients. We tried to create a service in providing useful information and updated data in the field of dialysis technology. We hope we have succeeded in providing a volume of both practical use and theoretical interest.

Giuseppe La Greca
Claudio Ronco