

**Nephrotoxicity**  
*In Vitro to In Vivo*  
**Animals to Man**

# **Nephrotoxicity**

## ***In Vitro* to *In Vivo***

### **Animals to Man**

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**BODIL SCHMIDT-NIELSEN**

## BODIL SCHMIDT-NIELSEN

It is often difficult to be certain whether hereditary or environment contributes most to those who establish a long list of scientific achievement. In the case of Bodil Schmidt-Nielsen both factors have contributed to make a very special person. As the daughter of August and Marie Krogh she inherited an enquiring mind and grew up in an environment where physiology and medicine were the day to day pulse. Throughout the rest of her life it has been places and people that played a major role in shaping her contributions to science; in particular comparative renal physiology.

Bodil Schmidt-Nielsen's basic training at the University of Copenhagen was in dentistry. She continued to complete a doctorate in odontology on the biochemistry of saliva, its formation and composition. These and other innovative studies resulted in her receiving an award from the King Christian 10th Fund for her work on the role of saliva in protection against carries.

She left her post as assistant professor at the University of Copenhagen and moved to the United States of America in 1946, where she became involved in studying excretory organs and particularly renal physiology. Over a number of years as research associate, assistant professor or professor she worked at Stanford, the Kettering Institute Cincinnati, the Department of Zoology at Duke University, and the Department of Biology at Case Western Reserve, where she was chairman in 1970, and adjunct professor from 1971 to 1975. Over these years her research interest had focused on fluid and electrolyte changes in species as varied as the amoeba, and fish, reptiles and the mammalian kidney. Shortly after her arrival in the United States of America she was invited to undertake research at the Mount Desert Island Biological Laboratory, Salsbury Cove, in Maine. It is here that the field of renal physiology and epithelial transport was associated with many of the giants amongst nephrologists. These included Homer Smith, E.K. Marshall, Roy Foster and others.

In 1971 she moved to the idyllic area of Salsbury Cove to undertake research at the **Mount Desert Island Biological Laboratory**, first as research scientist, then as deputy director in 1979, vice-president in 1980 and president from 1981 to 1985.

The Mount Desert Island Laboratory was incorporated under the state laws of Maine as a non-profit scientific and educational institute. While its original purpose was to teach undergraduates marine biology it has always been the focus of a vibrant research interaction between large numbers of researchers who use this unique location to study aquatic and non-aquatic animals to probe the wonders of kidney function. While much of the research focus at Mount Desert Island has been on normal renal regulation and function, the problems of increasing marine pollution has necessitated an orientation towards studying the effects of chemicals on these processes and now toxicology is an integral part of the research programme.

It is in the area of urea handling and water metabolism, particularly its adaptation under extreme situations such as the arid conditions experienced by the Kangaroo rat and the camel, that Bodil achieved her worldwide renown. She was awarded the John Simon Guggenheim Memorial Fellowship in 1953 for her work on the water metabolism of camels in the Sahara Desert.

Her immense contribution to research has been recognised by her being an established investigator of the American Heart Association, and the principal investigator of NIH training and research awards throughout her career. She was also president of the American Physiological Society, Associated Editor of the American Journal of Physiology, Council Member of the Society for Experimental Biology and Medicine, Fellow of the New York Academy of Science, Fellow and Council Delegate of the American Association for the Advancement of Science, Fellow of the American Academy of Arts and Sciences and Trustee of the Mount Desert Island Biological Research Laboratory. Bodil has authored over 250 scientific contributions and trained scores of life scientists and physicians. Few people linked to renal physiology or nephrology have not been influenced by her research or teaching.

Bodil Schmidt-Nielsen stands foremost in using a comparative approach to combine the assessment of renal function and morphology in different species. This is vital for the area of nephrotoxicity, where due to the cascade of events following a primary injury the changes in function are very often followed by changes in morphology and vice versa. In addition, it is most important to choose an animal model with renal speciality or attributes that provide a research handle, instead of making use of whatever is available, but may be inappropriate.

The comment that Bodil is a "very special person" is also supported by the fact that she gave the first Bowditch lecture in 1956. She was the first (and so far only) female president of the American Physiological Society and president of the Mount Desert Island Biological Laboratory. In retirement she continues to serve as an active member of a number of learned societies, attends and participates in international scientific meetings, takes the responsibility in directing future planning as a member of several boards of trustees and puts energy into writing overviews and reviews. She is also writing a long overdue biography of August Krogh and his Nobel Prize winning research, not only as a loving daughter, but also as an equal international scientist who can place her father's valuable contributions in perspective.

She lives a warm relationship with her husband, Roger Chagnon, friends and children and continues her long-term passionate love for the outdoors, where she will "out-walk or swim" many younger people. Research associates, friends and family know her as an accomplished vegetable gardener, an excellent cook and she is renowned for baking one of the best home-made breads in the State of Maine and probably much beyond. A very special lady!

Hilmar Stolte,  
Hannover,  
Federal Republic of Germany

## PREFACE

There has been a growing awareness that nephrotoxicity represents a key factor in human nephropathies, where, irrespective of the causative agent, only a few clinical end-effects are diagnosed. Thus nephropathies are generally classified as acute or chronic renal failure, malignancies or immunological changes. The weaknesses in diagnosing nephropathies arises because of the effective role the kidney plays in maintaining homeostasis, despite the fact that it has been extensively damaged.

The frequencies of some type of chemically-induced acute renal failure is well documented, but the causes of chronic renal failure, malignancy, and other nephropathies are far more difficult to associate with a chemical aetiology.

Many of the new therapeutic agents have important beneficial effects, but they are found to have marked nephrotoxic effects. Thus there is a growing urgency to increase the stringency of chemical safety evaluation for their potential nephrotoxic effects. This is strongly countered by the increased financial pressure to identify potentially nephrotoxic chemicals earlier in their development and humanitarian considerations to more closely relate animal test to the clinical situation. Part of the challenge may be achieved by the increasing use of in vitro techniques.

The objectives of this symposium have been to draw these central issues together and to try and establish where animal nephrotoxicity data is relevant to the clinical situation. If it is not, there is a need to define the factors that have to be considered to improve the validity of safety evaluation studies. Similarly, there is a need to define under what situation in vitro studies can effectively mirror the normally functioning kidney and replace the use of animals. Where these techniques currently have limitations new and innovative approaches are needed to better define the mechanism of renal injury and relate this to risk-benefit considerations in developing novel chemicals or using established substances under a diverse set of circumstances.

The Symposium could not have been organized without the contribution of the Scientific Advisory Committee, the Sponsors, and the secretarial support of Lisa Breitner, Laura Mellor, Mimps E. van Ek, Janet Williams and Sally Basford. The index was prepared by Enoch Kwizera.

Peter Bach  
Edward Lock

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