Kidney International, Vol. 18 (1980), p. 539

Introduction

The Symposium on Drug Effect on the Kidney was held in Sydney in October, 1979, under the sponsorship of the Australian Society of Nephrology and the Royal Prince Alfred Hospital. Renal pharmacology often is tacitly assumed to be almost synonymous with the pharmacology of diuretic drugs, for understandable reasons. Certainly these are the agents most often prescribed because of their renal site of action. But, in planning the symposium, it was considered desirable to focus on other types of drugs that act on the kidney. As the final program evolved, approximately two thirds of the papers were concerned with various aspects of nephrotoxicity. This emphasis was readily justified on two scores: its enormous importance in clinical medicine and the accelerated pace of interest in recent basic research. The remaining papers were concerned with a variety of other biochemical, physiologic, and pharmacologic problems.

Although the nature of clinical drug toxicity is widely recognized, the magnitude of the problem is difficult, if not impossible, to define. This applies to toxicity in general as well as to nephrotoxicity in particular. Many of the therapeutic problems that are involved have been covered in the symposium. These include the use of antibiotics, the chemotherapy of malignancy, the treatment of mental illness, the management of hypertension, the use of analgesics, the public health implications of over-the-counter sales, and several aspects of the impact of environmental pollutants on health.

The mechanisms of drug action vary from one tissue to another. Some of the factors peculiar to the kidney are discussed in detail and need not be repeated here. We mention, however, the recurrent statement that the kidney's vulnerability to the adverse effects of drugs is related to the exceptionally high renal blood flow. The concept is correct at one extreme to the extent that an avascular tissue would be relatively drug insensitive, and at the other extreme to the extent that there are some drugs, not a great many, that are completely removed or extracted by the kidney from the incoming arterial blood. In this instance, the renal blood flow can become the rate-limiting factor that determines the amount of drug to which the kidney is exposed.

For most drugs, however, the importance of renal blood flow involves its relationship to other renal mechanisms. The kidney has the capacity to filter an enormous volume of fluid at the glomerulus. There is also a large assortment of specific mechanisms for the transport of different drugs across the tubular epithelium. Both processes can increase the concentrations of drugs—the former when the rate of water reabsorption exceeds the rate of drug reabsorption, the latter when the transport process itself delivers the drug either into the tubular fluid or into the tubular cell. Additional factors must also be taken into consideration such as binding to plasma protein, the rate of urine flow, the pH of the urine, and the presence of analagous compounds that might influence transport.

A basic tenet of pharmacology is that drug action, either beneficial or toxic, depends on the concentration of drug in the neighborhood of receptors. We say "neighborhood" advisedly because often neither drug concentrations nor locations of receptors are known with certainty, particularly in the kidney. For a number of drugs, however, these questions are now being answered in relation to distribution both along the nephron as well as within the subcellular organelles.

We wish to thank the following companies and organizations for their financial support for visiting speakers: Merck Sharp & Dohme (Aust.) Pty Ltd., Eli Lilly (Aust.) & Co., Astra Chemicals Pty Ltd., Glaxo Group of Companies, I.C.I Australia Pty Ltd., Australasian Society of Nephrology, Ciba Geigy Aust. Ltd., Roche Products Pty Ltd., Upjohn Pty Ltd., Sandoz Aust. Pty Ltd., Waters Associates, Travenol Laboratories, and Abbott Aust. Pty Ltd. We also wish to thank the following companies for their financial support: Burroughs Wellcome & Co. Ltd., Smith Kline & French Ltd., Cyanamid Corporation, Boehringer Ingelheim Pty Ltd., Wm. S. Merrel Company, Nicholas Pty Ltd., Miles Laboratories, and Weddel Pharmaceuticals.

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Received for publication May 29, 1980
0085-2538/80/0018-0539 $01.00