Nephron *13:* 5–6 (1974)

Introduction

VICTOR E. POLLAK

Division of Nephrology, University of Cincinnati Medical Center, Cincinnati, Ohio

The association of proteinuria with abnormalities of the kidney was shown clearly by RICHARD BRIGHT well over a century ago. The role of the kidneys in plasma protein conservation and metabolism was studied from time to time thereafter, but it is only in the past two decades that the role of the kidney in plasma protein homeostasis, protein synthesis, and protein catabolism has been the subject of intensive investigation. Work by many investigators on the mechanism of protein excretion by the glomerulus, and on the role of tubular reabsorption and catabolism, has now given new insights into this problem.

This symposium was designed to summarize current thinking on the following questions:

(1) How does the glomerulus function as a molecular sieve?
(2) What is the fate of proteins which pass the glomerular filter?
(3) How does plasma protein concentration affect renal function?
(4) How can the proteins in urine be quantified and what is the meaning of various types of proteinuria?

The pioneering nephron puncture studies of BOTT and RICHARDS [1941] provided the first quantitative evidence of the efficiency of the glomerulus as a molecular sieve, which retains all but a minute fraction of the plasma proteins that traverse the glomerular capillaries. Electron-dense tracer proteins have been used extensively in recent years to investigate the ultrastructural basis of glomerular permeability. These investigations are reviewed by EVELINE SCHNEEBERGER, who concludes that both the mathematical models and the physiologic data favor the view that the glomerular basement membrane probably acts as a coarse filter for proteins, in series with a fine filter located in the slit pores.

Albumin and many plasma proteins of smaller molecular size that have been filtered by the glomerulus are reabsorbed by the tubules. Quantitative estimates suggest that more than 90% of the small amount of filtered albumin is absorbed, so that only a minute fraction appears in the urine. BOURDEAU and CARONE review this evidence and conclude that the proteins are absorbed by luminal endocytosis, and that they are then hydrolyzed by lysosomal enzymes. Their studies on isolated perfused tubules fail to show evidence for contraluminal uptake of albumin. Tubular reabsorption and hydrolysis by lysomal enzymes has now emerged as an important mechanism for the normal catabolism of many plasma proteins of small molecular size that have passed the glomerular filter, as STROBER and WALDMANN have shown.

An essential factor regulating renal function is the concentration of proteins in the plasma. KNOX and SCHNEIDER summarize the importance of the plasma proteins in the maintenance of plasma volume, which in turn regulates reabsorption by the renal tubule through renin-antiotensin aldosterone, and perhaps other natriuretic systems. They also review the evidence for the direct effect of plasma protein concentration on the rate of formation of glomerular filtrate, and on the uptake of reabsorbate from the renal tubules.

Protein handling by the kidney has been studied extensively in human disease in the past decade, and attempts have been made to predict the nature of the underlying renal disease from the results of differential protein clearances. These studies are reviewed by POLLAK, FIRST, and PESCE, who conclude that the protein clearance is best expressed in terms of the glomerular filtration rate, or sieving coefficient; and that the sieving coefficient is a useful physiologic index to differentiate proteinurias associated with glomerular or with tubular damage.

Many of the recent advances that have been reviewed for this Symposium would not have been possible were it not for the advent of the sophisticated, modern techniques of protein chemistry. These are reviewed in the final paper by AMADEO J. PESCE, who summarizes the application and limitation of each technique to studies in both the clinic and research laboratory.

Reference

BOTT, P. A. and RICHARDS, A. N.: Passage of protein molecules through glomerular membranes. J. biol. Chem. *141:* 291 (1941).