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Vol. 3

Clinical Nephrology

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Clinical Nephrology

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Volume 1. Physiology (Joseph S. Handler)
Volume 2. Morphology, Immunology, Urology (Robert H. Heptinstall)
Volume 3. Clinical Nephrology (E. Lovell Becker)

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Preface

A congress is a coming together. Like any 'happening', there is no accurate quantitative measurement for either its ingredients or its impact. If a congress is successful, one can choose to underline the depth and breadth of its planning, the diversity of its scope, the admixture of talented guests, the quality of presentation, the status of the science behind the presentation, the level of excellence in the particular scientific field, the interplay of personalities, the geographical setting, and even the weather. Judging from comments received, the III International Congress of Nephrology was a success. We hope that success is not measured merely by the 2134 scientists registered, the 624 abstracts submitted, or the 75 invited papers and 224 free communications presented. We hope that these tangible items are outweighed by the intangibles,—the new ideas appreciated, the constructive criticisms received, the new directions indicated, the new friendships created, and the old ones confirmed. The Congress served as a much needed worldwide inventory of the 'state of the art' of nephrology with its related basic and clinical components. It demonstrated the rapidity with which progress has been made in this remarkable new field of medicine.

In the beginning neither President BERLINER nor myself was in favor of publishing a Proceedings. The lead time for preparing presentations for international congresses is usually so long that publications are often dated or repetitious of already published work. In the end our minds were changed, as they should be, by the evidence at hand: the quality and breadth of the symposium presentations which represented a remarkable cross-section of the entire range of nephrology and the only currently available inventory of the field of nephrology as of 1966. The dramatic advances in dialysis and transplantation were matched by equally important additions in the basic fund of knowledge in related physiology, morphology, bacteriology, pharmacology, and immunology. The challenge of the kidney had obviously been a stimulating force in clinical investigation in the three years since Prague. So we have proceeded with these Proceedings which contain all but one of the invited presentations which comprised the symposia

at the Congress. We have divided them into three volumes, roughly designated as Physiology; Morphology, Immunology, Urology; and Clinical Nephrology. Those who were not able to attend the Congress and who have special interests may obtain the material of their choice from the publisher. For those who registered for the Congress, we hope that these three volumes will recall the happy and fruitful days of September, 1966.

For their work and cooperation we wish to express our sincere gratitude to the individual volume editors, Drs. JOSEPH S. HANDLER, ROBERT H. HEPTINSTALL, and E. LOVELL BECKER, to our Congress Manager, Mrs. HELENA B. LEMP, and to our publisher. Most of all, we wish to thank the authors, who deserve the real credit for writing these Proceedings of the III International Congress of Nephrology.

GEORGE E. SCHREINER, M. D.
Secretary-General
Coordinating Editor

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Maturation of the Neonatal Kidney

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The functional maturation of the kidney of the young infant has been of interest to nephrologists ever since BARNETT [2] demonstrated more than two decades ago that the rate of glomerular filtration in the newborn, despite correction for body size, is lower than in the older child or adult. Since then extensive data has been assembled pointing to limitations in other renal functions. It is of interest to review these data in terms of current concepts of renal physiology and renal regulatory mechanisms, to examine the functional status of the kidney with regard to the needs of the young infant, and to point out possible limitations that peculiarities of renal function in young infants may impose under conditions of stress.

An attempt will be made to develop the following four points:

(1) Compared with children and adults, renal tubular function in the infant is low;
(2) glomerular filtration rate is proportionately low, maintaining glomerulo-tubular balance;
(3) despite the quantitative limitation in renal function, renal regulatory mechanisms qualitatively are intact, providing adequately for the needs of the normal infant;
(4) as tubular mass increases and the heterogeneity of nephrons decreases, tubular functions and filtration rate increase, functional and anatomic maturation proceeding *pari passu*.

Functional and morphologic characteristics of the neonatal kidney will be reviewed. Special attention will be given to the renal mechanisms playing the major role in maintenance of body homeostasis, namely, reabsorption and excretion of sodium, diluting and concentrating mechanisms, and renal excretion of hydrogen ion. Without

attempting an exhaustive review, pertinent studies will be selected from the literature and data from a number of recent unpublished studies from our laboratory will be presented.

In Figure 1, glomerular filtration rate is plotted as a function of age. In contrast to most analyses of this type, glomerular filtration rate is presented as ml per min per gram of kidney. It can be seen that immediately after birth GFR is low, reaching mature levels at about one year of age. We might ask the question: 'Why is the GFR low?' It could be due to one of the following: inadequate systemic pressure for filtration; a thick, poorly permeable filtering membrane; or a small glomerular surface area for filtration. Low arterial pressure may play a role in the first few days of life, but it cannot be limiting beyond this period. It was thought at one time that the cuboidal epithelium of the glomerulus might limit filtration in the newborn, but this theory has been discarded. Microdissection data of FETTERMAN *et al.* [5] have demonstrated that the glomerular surface area (GSA) in the neonate is about $^1/_3$ that of the adult, whereas GFR is only $^1/_{12}$ that of the adult. Therefore, none of these three possibilities satisfactorily explains the low filtration rate.

Other morphologic data may be of help. In Figure 2, drawn also from data of FETTERMAN [5], the ratio of GSA to proximal tubular volume (PTV) is plotted as a function of age. Note that initially GSA or filtration area relative to proximal volume is high. As with GFR,

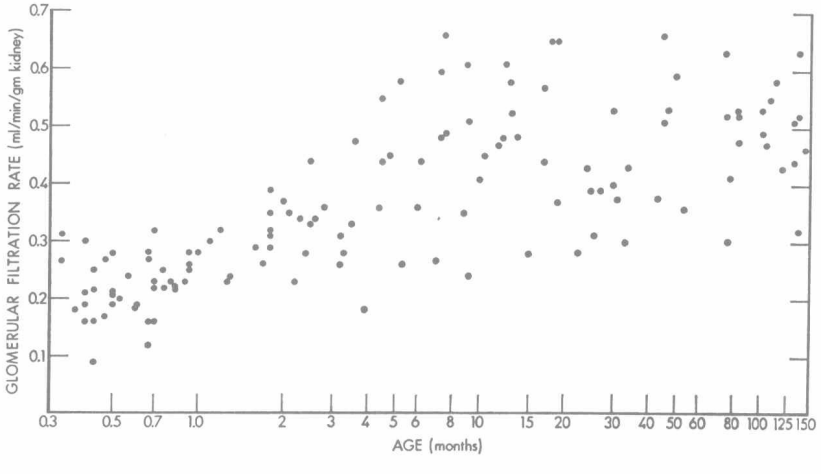

Fig. 1. Glomerular filtration rate in infants and children. Kidney weight was determined for each subject on the basis of body weight and height.

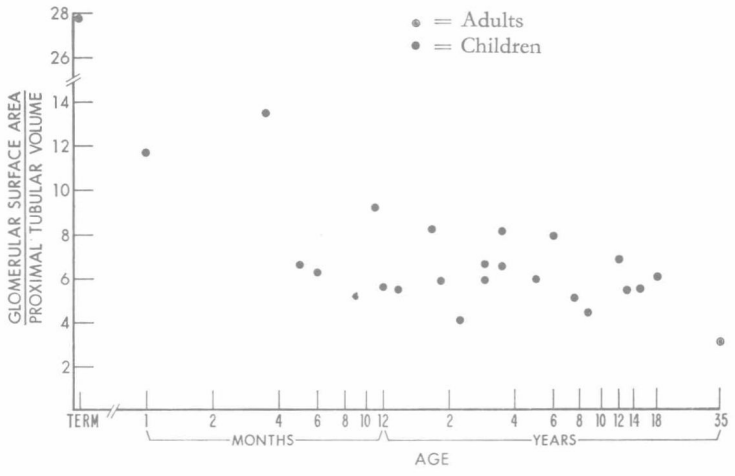

Fig. 2. Ratio of glomerular surface area to proximal tubular volume, determined by microdissection, related to age. Data are taken from FETTERMAN, *et al.* [5].

mature levels are reached by the end of the first year. Thus the potential area for filtration is relatively much greater than the actual filtration rate. If, as seems reasonable, PTV can be related to proximal tubular function, maintenance of a low GFR during this period serves to maintain glomerulo-tubular balance. At the end of the first year, as the ratio of GSA to PTV reaches mature levels, so also does the GFR. This correspondence provides evidence for the dependency of GFR on tubular function, GFR being limited during the first year of life to avoid overperfusion of a limited tubular system and glomerulo-tubular imbalance.

Another interesting and probably important morphologic feature of the neonatal kidney is the great degree of nephronic heterogeneity compared with that seen at a later age. In Figure 3 taken from the microdissection work of FETTERMAN [5], the distribution of various values for the ratio of GSA to PTV, termed r, is compared to the mean value of GSA to PTV for the entire kidney, termed R. Data from a group of adults is shown in the hatched area. The greater spread of values in the term infant is apparent. Note particularly the distribution to the right, indicating nephrons with high ratios of GSA/PTV.

We may speculate on the possible functional significance of these morphologic features. Certain deductions may be made as to the