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John A. Libertino, M.D.
series editor

Management of Vesicoureteric Reflux

Edited by
J. Herbert Johnston, M.B.

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Management of Vesicoureteric Reflux

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International Perspectives In Urology

EDITED BY
John A. Libertino, M.D.

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Series Editor's Foreword

In 150 A.D. Galen noted in postmortem studies that after tying the urethra and filling the bladder, no urine passed backwards up the ureters. This is probably the earliest recognition of the antireflux mechanism of the normal ureterovesical junction. Work in the early 1920s intimated the relationship between vesicoureteral reflux and the development of chronic pyelonephritis. It was not until 1958 that Victor Politano and Wyland Leadbetter published what was to become the standard technique for antireflux surgery. Shortly thereafter, the causative relationship between reflux and chronic pyelonephritis was established.

The pioneering work of Victor Politano not only led to the understanding and surgical treatment of vesicoureteral reflux but was the genesis for growth of pediatric urology.

The management of vesicoureteral reflux has been controversial from the outset. The role of antibiotic therapy and the indications and contraindications to reimplantation and reconstructive surgery are still hotly debated in the urologic literature. It is for this reason that we are particularly pleased that Mr. J. H. Johnston, a world authority in pediatric urology, is editing this book on vesicoureteral reflux. Mr. Johnston, who has made many of the major contributions in the field of pediatric urology, is particularly qualified to bring to us the most contemporary information available on the management of vesicoureteral reflux.

The task of editing a book of this nature is not an easy one. Mr. Johnston must be congratulated for bringing the best of Europe and America together in a collaborative fashion to crystalize the diagnosis and treatment of reflux. I hope that this contemporary monograph will be of benefit to both urologists and residents in training and to their patients who suffer from vesicoureteral reflux.

JOHN A. LIBERTINO, M.D.

Preface

So many men, so many opinions; everyone has his own fancy
Terence (185–159 B.C.) Phormio ii, 3, 14

A quarter of a century has elapsed since the late John Hutch drew attention to the damaging effects of vesicoureteric reflux with urinary infection on the renal parenchyma and since John Hodson described the urographic changes characteristic of reflux nephropathy and pointed out the deleterious influence of reflux on the growth of the kidney during childhood. During that period of time a veritable library of literature has accumulated on the subject, and an unbiased observer might expect that there would by now be general agreement on the matter and a universally accepted, orthodox approach to the management of the affected patient. However, even a superficial perusal of the journals or a casual audition of presentations at urological conferences will reveal the existence of varied, sometimes contradictory, views, even among experienced experts, indicating that we are still in the realm of individual opinions rather than of concrete facts. The reader who expects the final, conclusive answers to be revealed in the present volume will be disappointed; indeed, it will be seen that here, too, conflicting concepts are expressed. However, it is hoped that by airing the more important clinical aspects of the subject, some of which have not been discussed before in any depth, further study may be stimulated so that a definitive conclusion might eventually emerge as how best to treat the baby, the child, or the adult with vesicoureteric reflux.

J. H. JOHNSTON

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Contents

1

The Pathology of Reflux Nephropathy

M. J. Bouton

"Chronic pyelonephritis," "reflux nephropathy," and renal scarring" are terms that have been employed, more or less synonymously, without any clear definition of what was being described in strict pathological terms.

It would be wise to abandon the last two terms for the following reasons. First, there is much doubt as to whether reflux *per se* leads to any lesion of the kidney parenchyma; whereas Hodson *et al.* (1) maintain that sterile intrarenal reflux can damage the kidney, Ransley and Risdon (2) have shown that both infection and reflux are necessary to produce renal scars. Second, vesicoureteric reflux, as emphasized by Waterhouse (3) is a radiographic finding and not a diagnosis and is itself more often than not secondary to some other urinary tract lesion. Third, the histological changes that are claimed to have been produced by reflux are identical with those of "chronic pyelonephritis" as described later. The term "renal scarring" could again be usefully dropped because it is a misnomer. The depressed contracted area called a scar by analogy with the scar in subcutaneous tissue following a superficial wound (of the skin) is contracted not so much because of keloidal fibrous tissue contraction as in the skin, but because of loss of volume of tissue.

We are, therefore, left with defining the kidney changes in "chronic pyelonephritis." Grossly, the picture is a very familiar one; the kidneys are small and have an irregular surface with depressed areas. On sectioning, the parenchyma is much reduced in thickness with a net reduction in the ratio of cortical to medullary thickness. Characteristically, the depressed area of cortex overlies an abnormal, widened calyx. Microscopically (Fig. 1.1), the interstitium between the cortical tubules is infiltrated by lymphocytes and plasma cells, sometimes so intensely that germ cell follicles are found. The tubules show varying degrees of so-called "atrophy"—the epithelial cells tend to be flattened and the tubular basement membrane is thickened. Nonfunctioning of the tubules leads to accumulation of an eosinophilic material within the lumen—the so-called thyroid tubules—because of the superficial resemblance of a collection of such tubules to thyroid acini. Because of the loss of interstitium, glomeruli are crowded together and all stages of

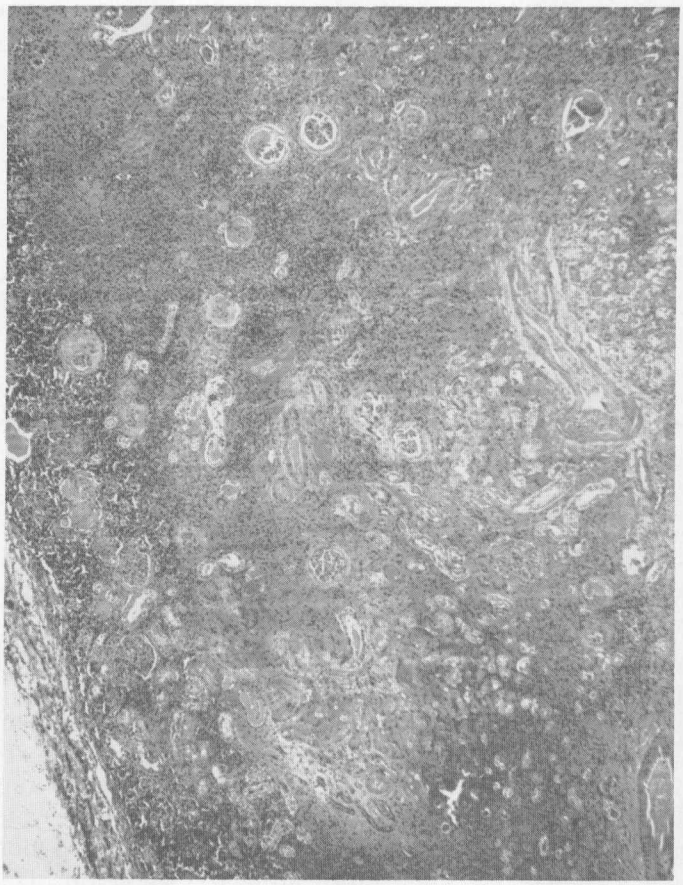

Figure 1.1 "True" pyelonephritis—male aged 10 years. Six-year history of recurrent urinary tract infection with reflux. Nonfunctioning left kidney excised. Note thickened capsule, hyalinized glomeruli, and lymphocytic infiltration of interstitium.

periglomerular sclerosis leading to complete hyaline bodies are found (Fig. 1.5). There is often inflammation of the wall of the underlying calyx (Fig. 1.2). It must be noted that, contrary to general opinion, there is no increase in fibrous tissue, either in the interstitium or in the glomeruli. Under the electron microscope there are no collagen bundles with their characteristic cross-banding in the interstitium, whereas the glomeruli show an increase in membranoid material being deposited in the mesangium and filling the capillary lumen. Blood vessels show a reduced ratio of lumen to wall thickness, and in more advanced cases intimal hyperplasia and replacement of the medial muscle by fibrosis are quite evident. These areas are well demarcated (Figs. 1.8 and 1.9), sometimes very sharply, from surrounding normal areas and never merge into areas of acute pyelonephritis, the changes of which are quite different, with pus in the lumen of the tubules and microabscess formation. What deductions can be derived from the above? First, the changes are essentially nonspecific, as emphasized by Farmer and Heptinstall (4). Different processes, *e.g.*, ischemia and obstruction will lead to the same result, particularly if the obstruction takes place during

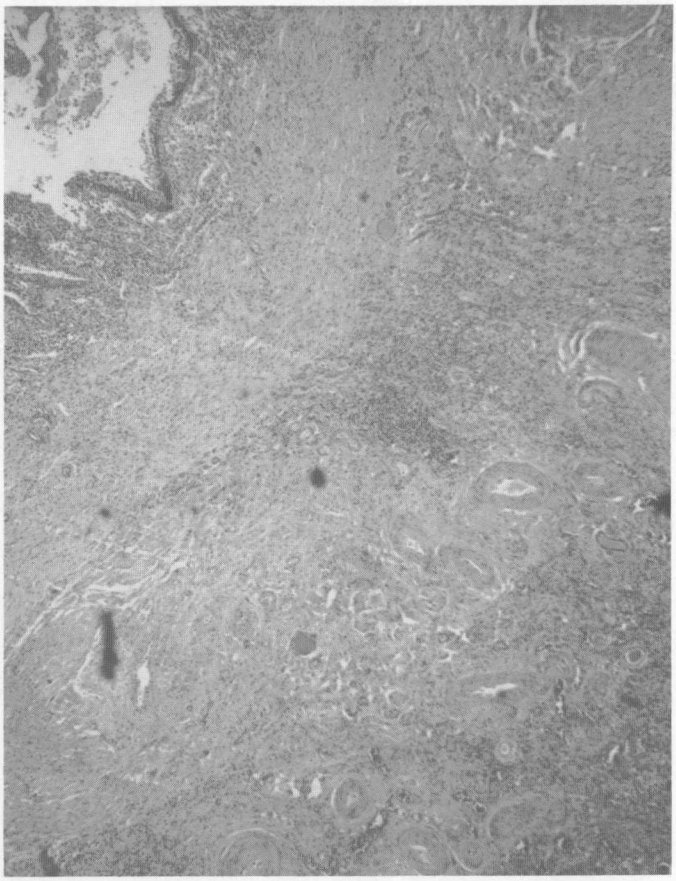

Figure 1.2 Same case as Figure 1.1. Inflammation of calyx underlying affected cortex.

organogenesis. Second, serious doubt must be entertained as to the bacterial origin of "chronic pyelonephritis," a point well argued by Schwartz and Cotram (5). They could find bacterial antigen in only one of nine affected kidneys selected under strict criteria for pyelonephritis, *i.e.*, scarring, calyceal deformity and inflammation, and the presence of normal glomeruli in unscarred areas. In contrast, antigen was found in three of five kidneys with acute pyelonephritis, and bacterial antigen was found to persist in renal scars secondary to experimental bacterial pyelonephritis. Third, and perhaps most important, is the close similarity of these changes to those of dysplasia. Bernstein (6) describes dysplasia as referring to the presence of microscopic abnormalities variously attributed to developmental arrest, to failure of differentiation and persistence of fetal structures, and to persistence of mesonephric tissues. For the diagnosis of dysplasia the following criteria are usually applied: (a) primitive ducts which are lined by tall epithelium (7) and surrounded by rings of connective tissue (Fig. 1.3), and (b) nests of metaplastic cartilage. The presence of either of these elements, which obviously represent aberrant developments from the metanephric blastema, presents no difficulty in recognition. However, other elements—primitive

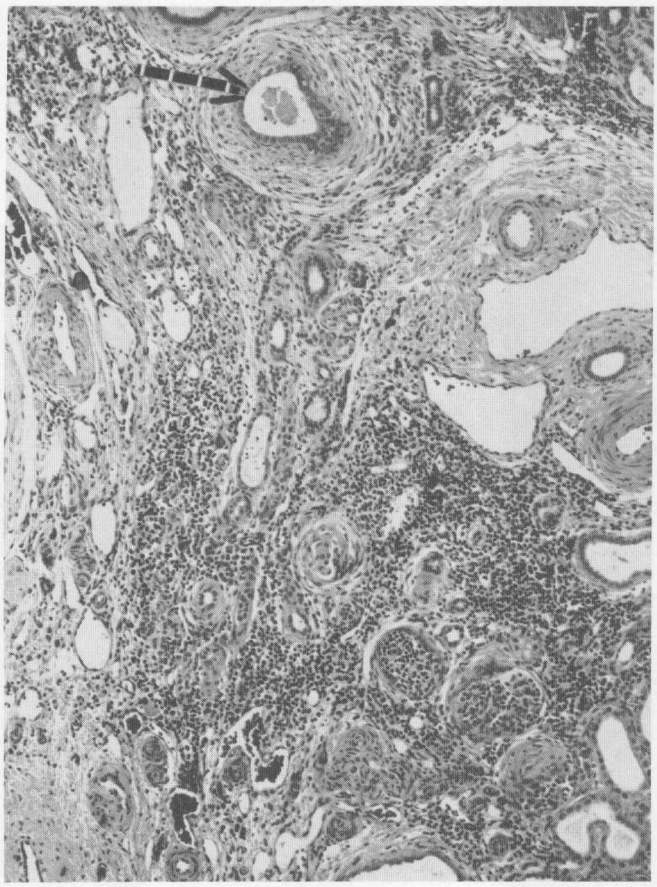

Figure 1.3 Pseudopyelonephritis. Nubbin of kidney drained by atretic ureter. In addition to hyalinized and hyalinizing glomeruli and lymphocytic infiltration, note abnormal tubule (*arrow*).

ductules and primitive tubules—which have a smaller lumen than that of the ducts and are lined by columnar epithelium may not be necessarily dysplastic in the full meaning of the word (8) insofar as they are not abnormally developed structures; they may well be alterations of normally developed structures as a result of an insult during nephrogenesis (Fig. 1.4). Bernstein (6) demonstrates convincingly that primitive tubules and ductules can arise as a result of obstruction to urinary flow and even of trauma during nephrogenesis. The practical importance of these theoretical considerations is that "chronic pyelonephritis" has undoubtedly been overdiagnosed in the past (9) and that its incidence was found to be markedly reduced in recent autopsy studies (10). In pediatric practice the clinical entity most frequently encountered goes under the name "primary atrophic pyelonephritis" or sometimes "nonobstructive pyelonephritis," the main features of which are an early onset (within the first 2 or 3 years), large "scars" in the cortex, and an associated vesicoureteric reflux. From the above discussion it is clear that neither bacterial infection nor reflux *per se* can be accepted as playing a primary role in the etiology. On the other hand, the importance of dysplasia has