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ORIGINALS

Renal Papillary Morphology and Intrarenal Reflux in the Young Pig

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Summary. Intrarenal reflux in piglets has been related to the morphology of individual renal papillae. These studies show that intrarenal reflux occurs only in the presence of the more extensively fused papillae found predominantly at the upper and lower poles of the kidney. These papillae each have a flattened or concave area cribrosa with large open papillary ducts which cannot be closed by a rise in intracalyceal pressure. In contrast intrarenal reflux never occurs into cone-shaped papillae seen most commonly in the mid-zone of the kidney, which have easily closed, oblique, slit-like papillary duct orifices. The significance of these findings in relation to the genesis of chronic pyelonephritic scarring is discussed.

Key words: Renal papillae, Intrarenal reflux, Reflux nephropathy, Chronic pyelonephritis.

Introduction

In children with gross vesicoureteric reflux, micturition pressure may force urine retrogradely into the tubular system of the kidney (7). This phenomenon of intrarenal reflux (IRR) has been proposed as a mechanism of renal damage resulting in the characteristic scar of chronic pyelonephritis (5).

Although IRR can be demonstrated radiologically in only 7 % of refluxing systems in children under 4 years old (10), it has been shown clinically (10) and experimentally (4) to be associated with a high incidence of renal scarring. When IRR occurs it affects only some segments of the parenchyma, usually at the poles of the kidney.

Using young pigs we have investigated a number of factors which might be concerned in the production of IRR. In particular, we have examined the morphology of the renal papillae both in segments of the kidney shown radiologically to be affected by IRR, and in non-refluxing zones.

Materials and Methods

Radiological Demonstration of IRR

Fourteen young Welsh piglets aged 1-91 days (median 32 days) were anaesthetised and each kidney in turn was exposed extraperitoneally. The ureter was mobilised and 2 fine polythene cannulae were inserted into the lower end. One cannula was passed upwards into the renal pelvis and connected via a transducer to a chart-recorder and a calibrated television display. The other catheter was used for injection and drainage. The blood pressure was monitored continuously with an arterial catheter. Using a lubricated plastic syringe Hypaque 45 % (sodium methylglucamine diatrizoate, Bayer) was injected into the ureter to produce a pressure wave form in the renal pelvis with a peak duration of 12-15 seconds simulating vesico-ureteric reflux. This was performed with peak pressures of 10 mm, 20 mm, 30 mm and 40 mm Hg (13 cm, 27 cm, 40 cm and 54 cm H_2O); radiographs of the kidney were obtained at the end of each 'refluxing' episode using a GR 300 mobile X-ray unit (Todd Research Ltd) and standard screen cassettes (Fig. 1).

Pathological Examination of the Kidneys

Each kidney was examined first in the fresh state (Fig. 2). The renal pelvis and calyces were opened, and the gross specimen photographed. After formalin fixation each individual renal papilla was stained with 1 % methylene blue to improve contrast and then photographed

Fig. 1. A radiograph showing the typical appearances of bipolar intrarenal reflux

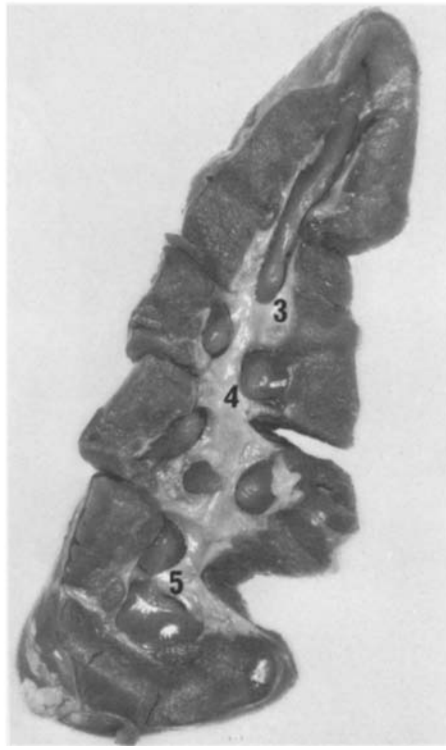

Fig. 2. The kidney depicted in Fig. 1 opened to display the renal papillae. The numbers refer to papillae illustrated in Figs. 3, 4 and 5 Magn. X 1.1

at a magnification of approximately X 20 using a Leitz 'Aristophot' (Figs. 3, 4 and 5)

Classification of Renal Papillae

Each renal papilla has a single area cribrosa and is either simple, when formed from a single pyramid, or compound, when the apices of several pyramids are fused. Simple papillae, which most closely resemble the traditional concept of a renal papilla, have a conical or domed tip bearing the area cribrosa. The papillary ducts open obliquely through small, often slit-like orifices (Fig. 4). Compound papillae are of three types. Type I papillae result from fusion of two, or rarely three pyramids at their tips. Apart from their larger size, these papillae closely resemble the simple variety, particularly with regard to the convexity of the area cribrosa and the manner by which the papillary ducts open. Type II papillae represent fusion between two or three pyramids which are, however, still identifiable as separate units. The area cribrosa forms a valley-like depression of varying depth between the component pyramids. Although the papillary ducts open obliquely near the margins of the area cribrosa, at its centre they tend to open directly onto its surface through larger, round or oval orifices. Through these central orifices the first generation of collecting ducts are sometimes visible (Fig. 5). Type III papillae are more completely fused, and often derived from three, four, or even more pyramidal units arranged into complex ridges or 'fleur-de-lis' formations. The common area cribrosa is either flat or forms a shallow concave depression. Papillary duct openings resemble those of Type II papillae (Fig. 3).

Correlation of Radiological and Morphological Data

Radiological studies were performed in 14 piglets, on both kidneys in 11 and on one kidney in 3. These 25 kidneys were examined pathologically so that the occurrence of IRR could be related to the morphology of the renal papilla concerned. In each kidney the papillae draining the upper third (upper pole), middle third (mid-

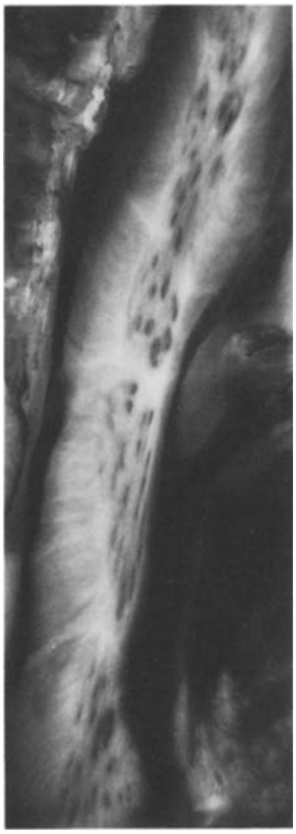

Fig. 3. Upper pole compound type III papilla associated with intrarenal reflux (cf. Fig. 1) Magn. X 7.2

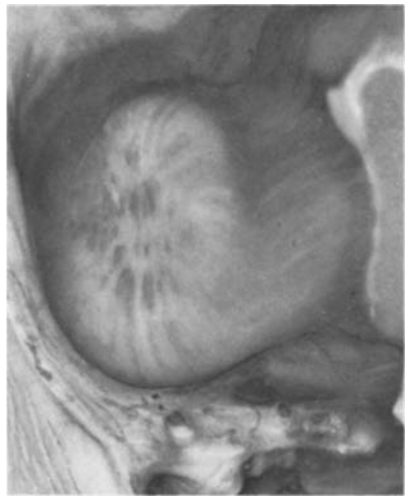

Fig. 4. Mid-zone simple papilla not associated with intrarenal reflux (cf. Fig. 1) Magn. X 7.2

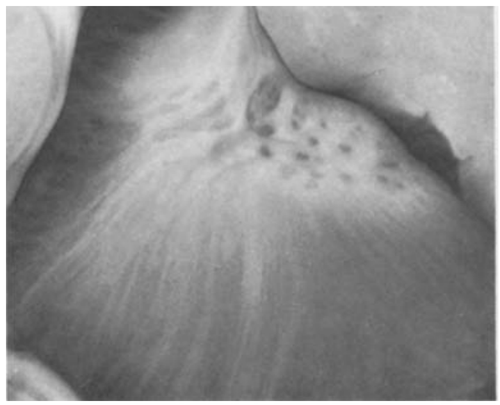

Fig. 5. Lower pole compound type II papilla associated with intrarenal reflux (cf. Fig. 1) Magn. X 7.2

zone) and lower third (lower pole) were identified on the radiograph and then on the macroscopic photographs of the gross specimen. Each papilla was then classified using the individual photograph of that papilla, and a note made of the number of constituent pyramids.

Results

The distribution of the types of papillae, and correlation of the radiological and morphological findings are shown in Tables 1 and 2.

Intrarenal reflux of some extent was present in every kidney examined, but occurred only in areas drained by compound papillae of types II and III, and never in areas drained by simple or type I papillae. Compound papillae of types II and III associated with IRR were much commoner at the upper and lower poles, whilst non-refluxing simple and type I papillae occurred predominantly in the mid-zones.

Table 1. Papillary numbers and distribution of papillary types in 25 pig kidneys

	Simple and compound type I	Compound type II	Compound type III
Upper pole	6	21	26
Mid-zone	76	19	2
Lower pole	7	21	14
Total	89 (46 %)	61 (32 %)	42 (22 %)

Table 2. Correlation of radiological and morphological data in 25 pig kidneys

Papillary type	Associated with IRR	Non-refluxing	Total
Simple and Compound I	0 (0%)	89 (100%)	89
Compound II	44 (72%)	17 (28%)	61
Compound III	36 (86%)	6 (14%)	42

Discussion

Although the association between chronic pyelonephritic scarring and vesicoureteric reflux (VUR) in children is well recognised (6, 11), the precise way in which renal damage occurs is not clear (1). However, recent clinical (10) and experimental (4) observations strongly suggest that severe reflux with pyelotubular extension (IRR) is the major factor determining scar formation, either by allowing pathogenic organisms access to the renal substance, or by hydrodynamic effects alone (5, 2).

Williams (14) suggested that in children with reflux, the difference between cases with chronic pyelonephritis and those without segmental scar formation might lie in local defence mechanisms at the renal papilla. We have examined this possibility more closely, and in particular we have sought differences within the same kidney between papillae subject to IRR and those which do not reflux. The piglet was chosen as an experimental model because, unlike any other laboratory animal, the pig has a multipapillary kidney resembling that of the human (12).

There is no clinical data available on the renal pelvic pressure generated during an episode of VUR. However, experimental studies in dogs show that the pressure in the renal pelvis closely follows bladder pressure where there is free reflux, especially when a megaureter is present (a common finding in children with severe VUR) (8, 9). Voiding pressures in children are high (3) and are not affected by reflux (15). Our pigs' kidneys were subjected to a range of pressure transients simulating a voiding pressure wave with peak values up to 40 mm Hg (54 cm H_2O). This falls well within the normal range for voiding pressures in childhood of 19-136 cm H_2O (14-100 mm Hg) determined by a number of workers (3).

Our results indicate that IRR is an "all or none" phenomenon. Areas of IRR associated with a particular papilla were visible as soon as the peak intrapelvic pressure exceeded 20 mm Hg (27 cm H_2O). Increasing the peak intrapelvic pressure merely increased the radiodensity of zones of IRR already present, but did not produce new areas of IRR from non-refluxing papillae. Similarly, variations of other factors such as blood pressure, intrarenal pressure and urine flow rate affected the intensity of IRR at any given intrapelvic pressure, but not its occurrence at any one papilla.

Our results suggest that IRR in the piglet depends primarily on the morphological characteristics of the papilla concerned. A type II or III compound papilla with a flat or concave area cribrosa, and open papillary duct orifices permits IRR, whereas a cone-shaped papilla with oblique, slit-like papillary duct openings does not. A suggested explanation is that the obliquely-orientated duct orifices would be easily closed by a rise in intrapelvic pressure, producing a "check valve" effect so that reflux does not occur. In contrast, large open papillary ducts situated on a concave surface cannot be closed by a pressure rise and once the pressure gradient between the calyx and the collecting system is reversed, retrograde flow can occur. The classification of papillae which we describe is based primarily on their overall shape, and in general this determines the pattern of papillary duct openings. Some type II and III papillae were encountered in which open central duct orifices were not a conspicuous feature and, as our results indicate, a fifth of type II and III papillae were not associated with IRR. On the other hand, open duct orifices were never seen on a convex papillary surface, and IRR never occurred with simple or type I papillae.

Studies of the fetal and mature human kidney have shown that the component lobes are arranged in 2 vertical rows (13). Although fusion between adjacent anterior or adjacent posterior lobes can occur anywhere within the kidney, fusion across the coronal plane only occurs in the polar regions where a single calyx may represent the fusion of up to 6 renal lobes. Examining the papillae in our pig kidneys a simi lar pattern emerged, and the more extensively fused refluxing type II and III papillae were situated mainly in the upper and lower thirds of the kidney. This distribution would explain the predominantly polar incidence of both IRR, and by inference, of chronic pyelonephritic scarring.

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