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Glandular Neoplasia within the Urinary Tract. The Aetiology of Adenocarcinoma of the Urothelium with a Review of the Literature

I. Introduction: The Origin of Glandular Epithelium in the Renal Pelvis, Ureter and Bladder

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Summary. The origins of glandular lesions within the urinary drainage tract are discussed, and their development by metaplasia of the urothelium illustrated. Illustrative cases show the development of cystitis cystica and cystitis glandularis: and their relationship to calculi, *Esch. coli* cystitis, *Schist. haematobium* infestation, and tumours under the Urothelium are discussed.

Although the regional division of the urinary passages into renal pelvis, ureter, and bladder is of clinical importance, it is of little real significance to the pathologist as the whole tract is lined by an essentially similar epithelium, and the epithelial tumours follow a similar overall pattern. The urinary passages are lined by a transitional stratified epithelium—the urothelium—and the usual epithelial tumour is a papillary transitional cell carcinoma. Adenocarcinoma is seen occasionally in the urinary bladder, the overall incidence being somewhat less than 1% of all bladder tumours (Thomas, Ward, Williams, 1971); and rather less frequently in the renal pelvis and ureter. The aetiology of adenocarcinoma of the urothelium has long been a field of dispute amongst urologists and pathologists, and in this respect the tumours of the whole urinary tract can be considered under one head. It should not be assumed, however, that adenocarcinoma found in a biopsy of the bladder is necessarily of primary urothelial origin. The Table lists a number of instances which can give rise to glandular neoplasia in a biopsy sample from the urothelium.

Group A—secondary carcinoma—accounts for an appreciable proportion of all cases and should always be excluded before assigning primary origin to the urothelium.

Group B—metaplasia within pre-existing transitional cell tumours—represents an ill defined group. Pugh (1959) and Sandrey (1967) stress the frequency of this phenomenon, and suggest 8–10% of all bladder tumours as the proportion showing some degree of adenomatous metaplasia. This is of importance in that the tumours behave biologically as transitional cell tumours, and should be treated as such.

Group C—represents the true vesical adenocarcinoma.

Group D—the urachal adenocarcinomas—is usually considered with the true vesical tumours (Group C) although their aetiology, and treatment, is different (Thomas, Ward, and Williams, 1971).

Table. *Glandular neoplasms in the urinary tract*

A. *Metastatic* or invasive carcinoma
—from rectum
prostate
ovary
uterus

B. *Metaplasia* within a preexisting transitional cell carcinoma

C. *Carcinoma* in *Metaplastic urothelium*
1) normally sited urothelium
2) in ectopia vesicae

D. *Carcinoma in embryonic rests or vestiges*
1) urachus
2) "mesonephric adenoma"

E. *Endometriosis*

Group E represents a rare finding but is included here to complete the picture. The majority of cases of endometriosis causing urinary symptoms do so by obstruction from the outside and do not involve the mucosa.

Material and Methods

The clinical material is drawn from the surgical and autopsy files of the United Sheffield Hospitals and hospitals of the Sheffield Regional Hospital Board.

5 μ sections from paraffin embedded material were stained with Haematoxylin and Eosin (H & E), Periodic-Acid-Schiff (PAS), Southgate's Mucicarmine, Gomori's Acid-Phosphatase method.

Clinical Cases

Case I. Male aged 49 who gave a 28 yr history of renal calculi and pyonephrosis. Histology of the renal pelvis at nephrectomy showed extensive glandular metaplasia. The metaplastic epithelium showed well developed mucus secreting acini without a muscularis mucosa (Fig. 4a). Paneth cells were not seen. There were interspersed areas of squamous metaplasia.

Case II. Male aged 40 with a history of right loin pain for many years. Rt. nephrectomy for renal calculus. Histologic examination of the renal pelvis showed complete replacement of the urothelium by a glandular epithelium (Fig. 4b) resembling that of the colon but without a muscularis mucosa. Paneth cells were not seen.

Case III. Male aged 64 with a history of Lt. renal pain for many years. Lt. nephrectomy performed for pyonephrosis and calculus. Histologic examination of the renal pelvis shows squamous metaplasia and some abortive gland formation. The ureter shows marked ureteritis cystica and ureteritis cystica glandularis (Figs. 1 and 2). The "normal" urothelium of the ureter contained amounts of mucicarmine positive material.

Case IV. Female aged 28 was admitted with a three week history of frequency, dysuria, and slight haematuria. Urine culture gave a pure growth of *Esch. coli.* Cystoscopy revealed a polypoid mass $1 \times 1.5 \times 1.5$ cm in relation to the right ureteric orifice. This was excised by cystodiathermy. Histologic examination showed polypoid cystitis glandularis with mucus secreting epithelium continuous with normal urothelium (Figs. 3, 5b). There was no abrupt change in epithelial type, but a gradual transition from normal urothelium to one of mucus secreting type with numerous goblet cells. There was only minimal inflammatory reaction. Follow up cystoscopies over the subsequent 5 years have shown no recurrence.

Case V. Male aged 13 was admitted with acute retention. Cystoscopy revealed a small polypoid mass at the internal urinary meatus which bled profusely when touched. Biopsy showed acute inflammatory changes together with cystitis cystica (Fig. 5a) and glandular metaplasia of the surrounding transitional epithelium, and the formation of glandular pseudopolyps. Urine culture yielded an almost pure growth of *Esch. coli.*

Case VI. Male aged 67 presented with dysuria and frequency of 3 months duration. He gave a history of previous *Schistosoma haematobium* infestation. Cystoscopy revealed a granular red plaque in the region of the trigone. Biopsy showed acute inflammatory changes with cystitis cystica (Fig. 8a) and cystitis glandularis (Fig. 8b). No ova of *Schistosoma* were seen, and the urine was sterile on culture.

Case VII. 8 years old Labrador dog was submitted for examination because of persistent haematuria. Bimanual examination followed by cystotomy revealed two papillary tumours on the ventral or anterior wall, each $3 \times 2.5 \times 2$ cm attached by narrow pedicles. These were removed with a cuff of bladder musculature. Histologic examination showed predominantly papillary transitional cell carcinoma with a high mitotic rate and marked nuclear pleomorphism. Much of the tumour exhibited a pseudo-adenomatous pattern with PAS positive material in the centre of pseudoacini (Fig. 6). There was evidence of tumour invasion of the muscularis. The adjacent urothelium showed prominent cell nests with central degeneration giving an appearance similar to cystitis cystica. There was no evidence of true glandular metaplasia.

Case VIII. Female aged 62 who presented with terminal haematuria. Cystoscopy revealed a fungating mass in the apex of the bladder. Bimanual examination showed this mass to be continuous through the bladder wall with a supravesical tumour. Partial cystectomy. Histologic examination showed colloid carcinoma of urachal type. The adjacent urothelium showed cystitis cystica and cystitis cystica glandularis but no intestinal-type metaplasia (Fig. 7a). Alive and well with no recurrence after 6 years.

Case IX. Male aged 65 admitted with blood and mucus in the stools and terminal haematuria. Cystoscopy showed a papillary tumour in the trigone of the bladder. Sigmoidoscopy showed an ulcerating neoplasm on the anterior rectal wall at 10 cm. Total excision of rectum and bladder. Histologic examination showed a moderately differentiated adenocarcinoma arising in the rectal mucosa and growing through into the bladder. The overlying urothelium showed cystitis cystica (Fig. 7b).

Discussion

Embryology and Normal Histology

The bladder has both endodermal and mesodermal origins, whilst the ureter and renal pelvis are wholly mesodermal in derivation. The bladder is formed from the vesico-urethral canal and the attached allantois, with the trigonum vesicae being formed in part from the absorbed common excretory duct. The allantois gradually regresses during intrauterine life so that it remains as an epithelialised connective tissue strand—the urachus. Abnormalitieis in the closure of the allantois result in the formation of urachal cysts and rests (Hamilton, 1952; Begg, 1931).

The epithelium of the urinary tract has origin from two germ layers. The epithelium of the renal pelvis, ureter, and possibly the trigone of the bladder are of mesodermal origin, whilst that of the remainder of the bladder is of endodermal origin. The whole of the urinary drainage tract is lined by a transitional stratified epithelium, or *Urothelium* (Melicow, 1945), varying only in thickness, from 2–3 cells thick in the renal pelvis to 5–6 cells thick in the bladder. The surface layer of cells contains diastase resistant PAS positive material (Mende and Chambers, 1957), and this may increase in inflammatory states (Fig. 1a).

The urothelium retains an enormous potential to undergo metaplasia into either a squamous or a glandular epithelium (Mostofi, 1954). Cystic and glandular metaplasia are seen predominantly in cases of calculus (Krag and Alcot, 1957); long standing chronic infection, particularly due to *Esch. coli* (Pugh, 1959) and schistosomiasis (Makar, 1957); and in exstrophy of the bladder (Abehouse, 1943). Although the urothelium is usually described as being devoid of glands, mucous glands have been described in the region of the trigone in middle aged and elderly patients (Albarran, 1892). These may represent metaplastic changes in the trigonal urothelium (Melicow, 1955) or be related to the paraurethral glands. Aschoff (1894) considered that they represented aberrant prostatic glands, but there seems little support for this hypothesis. Johnson (1957) showed that the renal pelvis in the horse had a partially glandular epithelium. Saphir and Kurland (1939) described tubular structures in the submucosa of the bladder apex in nine out of ten specimens examined, and Begg (1931) emphasised the prevalence of urachal remnants in the apex of the bladder. Subsequent authors have shown that the terminal few centimetres of the urachus remain patent in a significant proportion of cases. Mende and Chambers (1957) suggested that the change to a glandular type epithelium was due to a heightening of activity of cells that normally elaborated a mucoid material.

Cystitis cystica and Cystitis glandularis

Epithelial proliferation, through cystic change, to a glandular epithelium is an example of the metaplastic potential of the urothelium, and is seen in response to chronic irritation and long standing infection at any point in the urinary drainage tract; being graced with differing geographic names dependant on its exact situation: *pyelitis cystica*, *ureteritis cystica*, or *cystitis cystica*.

The initial change is one of epithelial proliferation with downgrowth into the submucosa (Fig. 1 b), the bud breaking free from the surface epithelium to lie as an isolated *cell nest* in the submucosa (Fig. 1 c). This point was contested by Stirling and Ash (1941) who claimed to show by serial section techniques that the epithelial nests retained continuity with the surface epithelium. The cell nest then undergoes central liquefaction with or without the production of mucus (Fig. 2 a, b) to produce the classic picture of *cystitis cystica* (Fig. 2 c, d, 5 a). The peripheral cells atrophy and the central ones desquamate to leave a cyst wall 2–3 cells thick. The innermost layer of cells reorientates with basal nuclei and assumes mucus secreting properties. This stage of the process has been termed *Cystitis cystica glandularis* (Fig. 3 a). The process may progress further to leave a single layer of cells with pronounced mucus production and even occasional Paneth cells (Gordon, 1963), *Cystitis glandularis* (Figs. 3 b, 5 b); the similarity between this and colonic mucosa is striking, although a muscularis mucosa is absent.

The development of Brunn's nests in response to chronic irritation and the progression to cystitis cystica was elegantly portrayed in a series of experiments by Giani (1906, 1907). A similar state of affairs can be seen in the renal pelvis in relation to calculi and pyonephrosis where there is often glandular (Case I and II, Fig. 4) (Paschkis, 1912; Brutt, 1924; Torassa, 1948; Krag and Alcott, 1957), as well as squamous, metaplasia, and neoplasia (Aiken, 1955). Many

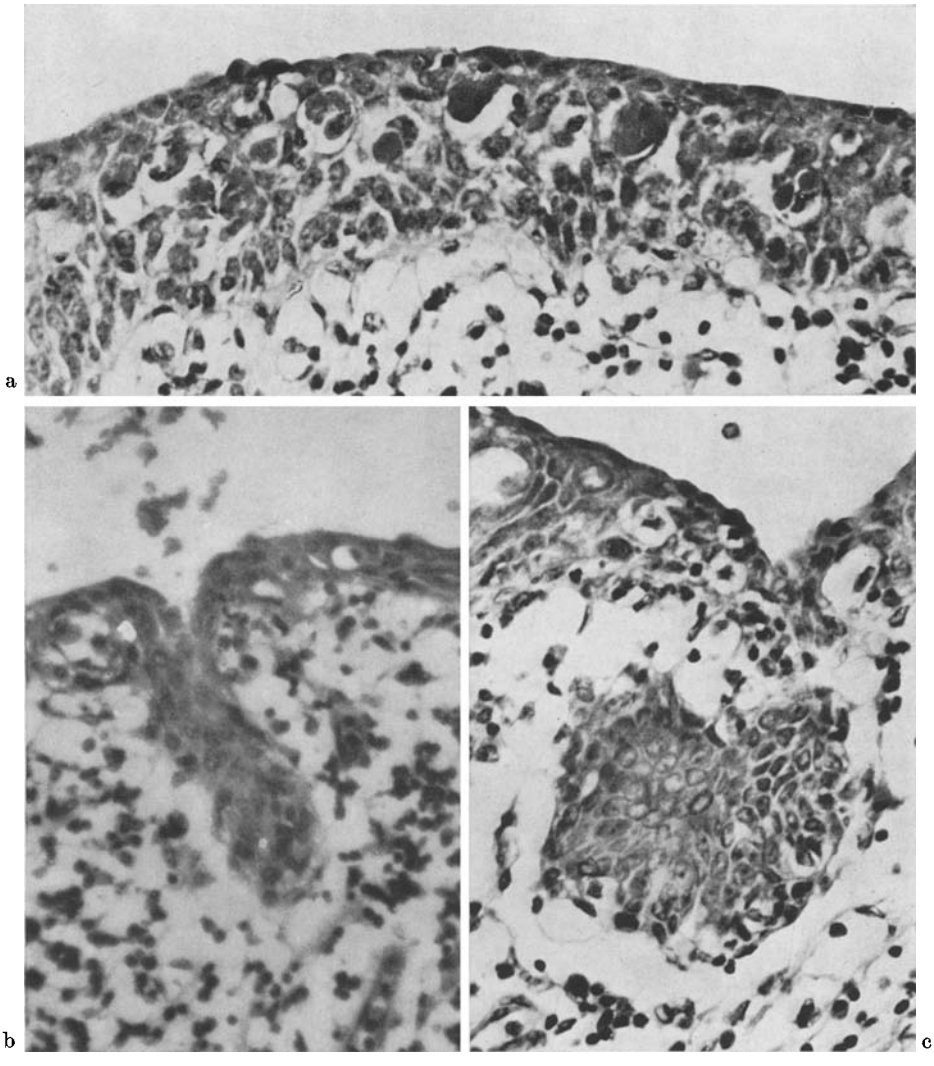

Fig. 1. a Case III, Ureteric epithelium containing PAS positive droplets. Periodic Acid-Schiff, mag. × 310. b Case III, Epithelial downgrowth. Haematoxylin and Eosin, mag. × 220. c Case III, Subepithelial cell nest, von Brunn's nest. H. & E., mag. × 310

authors, notably Patch and Rhea (1935), Mostofi (1954) and Kittredge and Brannan (1959), have demonstrated this metaplastic potential of the urothelium in response to chronic inflammation. The further potential of this metaplastic epithelium is the subject of considerable argument. Kittredge and Brannan (1959) and Grieve (1965) have shown that these lesions can be reversible, but Patch and Rhea (1935), Nesbit (1956), de la Pena *et al.* (1959), Salm (1967), Mostofi (1968), and Parker (1970) have emphasised their neoplastic potential.

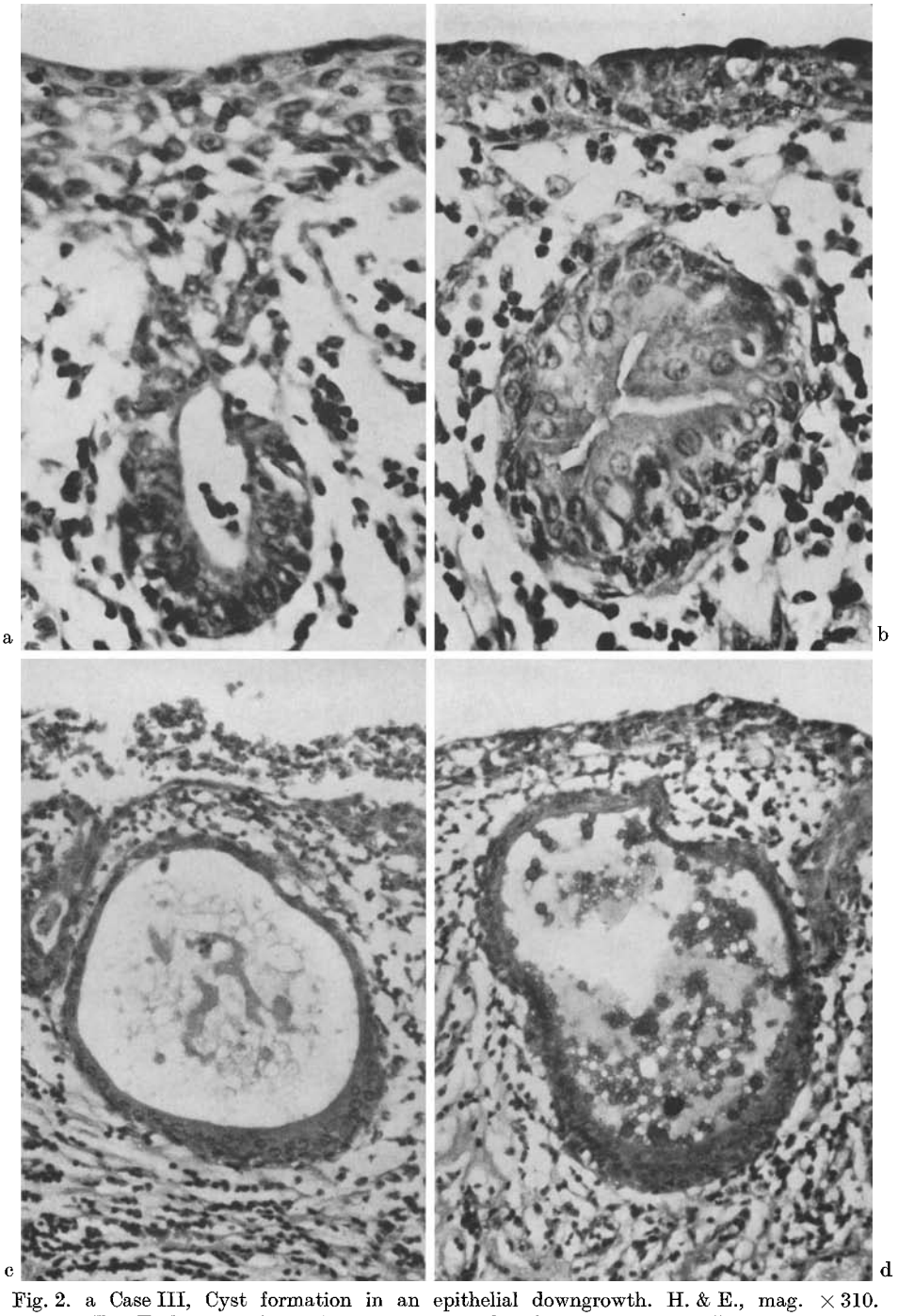

Fig. 2. a Case III, Cyst formation in an epithelial downgrowth. H. & E., mag. × 310. b Case III, Early cyst formation in a subepithelial cell nest. H. & E., mag. × 310. c Case III, Cystitis cystica. The cyst contains some flocculent proteinaceous material. Cystitis follicularis is also present deep to the cyst in the submucosa. H. & E., mag. × 170. d Case III, Cystitis cystica showing prominent protein aggregates in the cyst cavity. PAS, mag. × 170

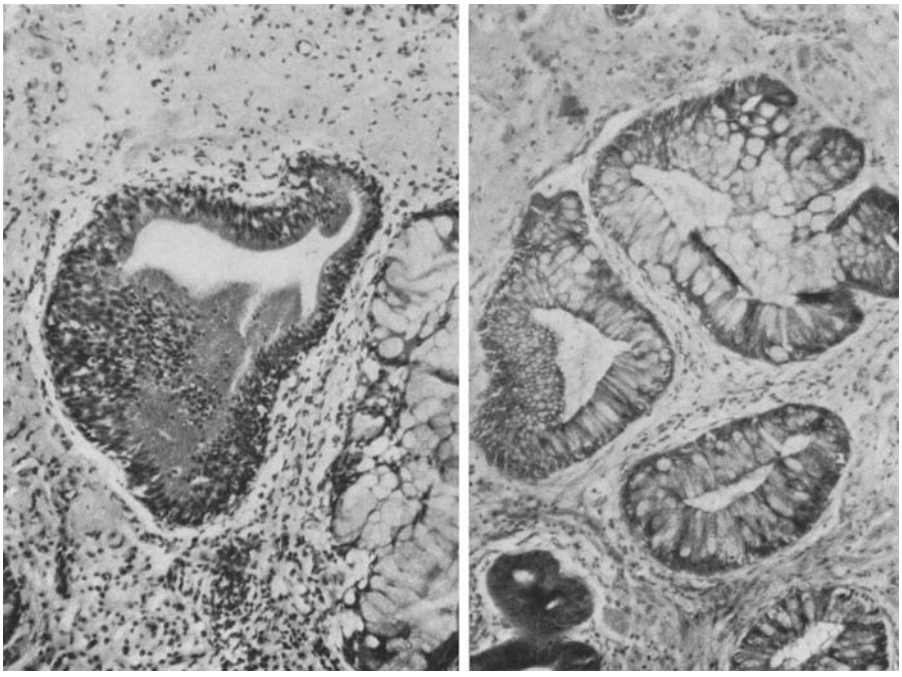

Fig. 3. a Case IV, Cystitis cystica glandularis. Transition phase to true glandular metaplasia. Nuclei are beginning to be arranged basally and PAS positive material is present within the cells. PAS, mag. × 95. b Case IV, Cystitis glandularis. H. & E., mag. × 85

Perhaps the best example of glandular metaplasia is seen in exstrophy of the bladder. In exstrophy much of the transitional epithelium is replaced by either squamous or glandular epithelium, squamous epithelium lying over glands in the submucosa. This metaplastic process is brought about as a result of chronic inflammation and irritation of the exposed mucosa, as well as the ever present risk of the mucosa dying because of exposure to the air. It was originally thought that the glandular epithelium was a developmental anomaly of the same aetiology as the exstrophy, but Enderlen (1904) and Formiggini (1920) showed that the epithelium was urothelial at birth and that the glandular epithelium arose by a process of metaplasia over a period of time. Scholl (1922) showed that the amount of glandular epithelium was roughly related to the age of the patient.

Glandular Metaplasia and Calculi

Although Morgagni (1760) noted that the irritation from a calculus incited the pelvis of the kidney to produce mucus, pyelitis glandularis appears to be a rarity if cases recorded in the literature are any indication. Towers (1963) demonstrated a case, but there are few fully documented cases in the literature. Paschkis (1912) illustrates two cases, as well as one of ureteritis glandularis, Brutt (1924), Torassa (1948) Krag and Alcot (1957) and Aiken (1955) one case each. Cases I and II illustrate this relationship, whereas Case III illustrates the reaction

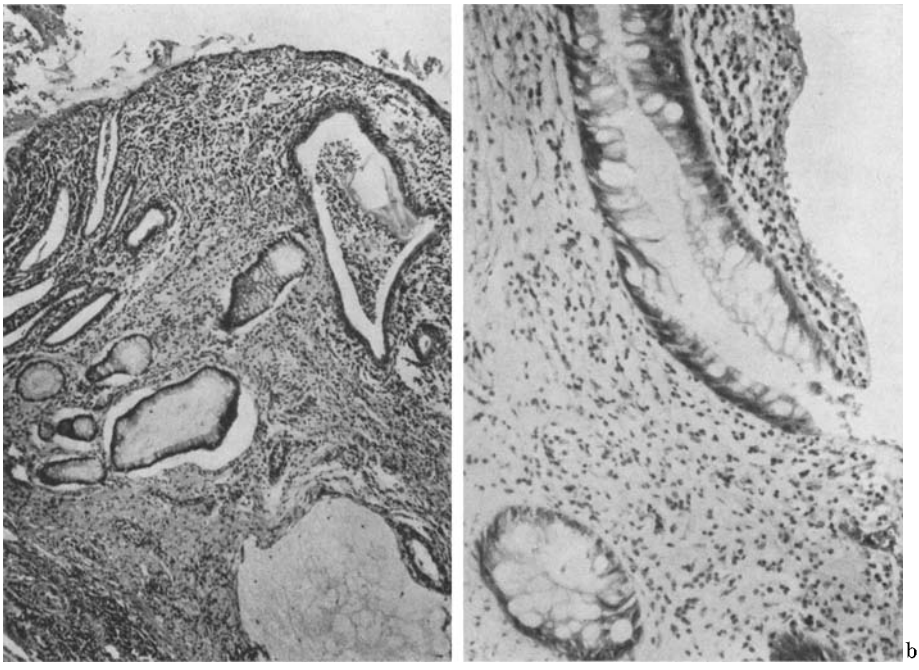

Fig. 4. a Case I, Pyelitis glandularis and acute inflammation of the submucosa. Squamous metaplasia can also be seen. H. & E., mag. × 35. b Case II, Isolated mucous glands in the renal pelvis without evidence of any muscularis mucosae. H. & E., mag. × 95

of the ureteric mucosa to infection and calculus in the renal pelvis. Brutt's case is unique in not being associated with a renal calculus. Glandular metaplasia in the renal pelvis is almost exclusively associated with calculus and chronic infection leading to pyonephrosis. Baker (1947) described a case of ureterocele with ureteric calculus and ureteritis glandularis. In the bladder the association is not so marked although one of the earliest recorded cases of vesical adenocarcinoma (Sharp, 1896) gives a history of previous lithotomy for calculus. Feldman (1930) described a papillary adenoma of the bladder in a 4 year old Hereford cow with multiple vesical calculi.

Metaplasia at any site occurs as a result of some abnormal circumstance or chronic irritation, as in squamous metaplasia of the bronchial epithelium and of the gallbladder in cholelithiasis. In both these situations the metaplastic epithelium is prone to neoplastic change if the inciting stimulus is not removed. Metaplastic epithelium can, therefore, be said to have a certain malignant potential. Such is the case with the glandular epithelium in the renal pelvis, and probably also in the ureter and bladder. There is a recognised association between cystitis cystica, leukoplakia, and squamous carcinoma of the bladder, and between glandular metaplasia, be it pyelitis glandularis or cystitis glandularis, and adenocarcinoma. Calculi and glandular metaplasia can be seen in 17 of the 22 cases of adenocarcinoma of the renal pelvis recorded in the literature, and in 5 of the 10 cases of adenocarcinoma of the ureter.

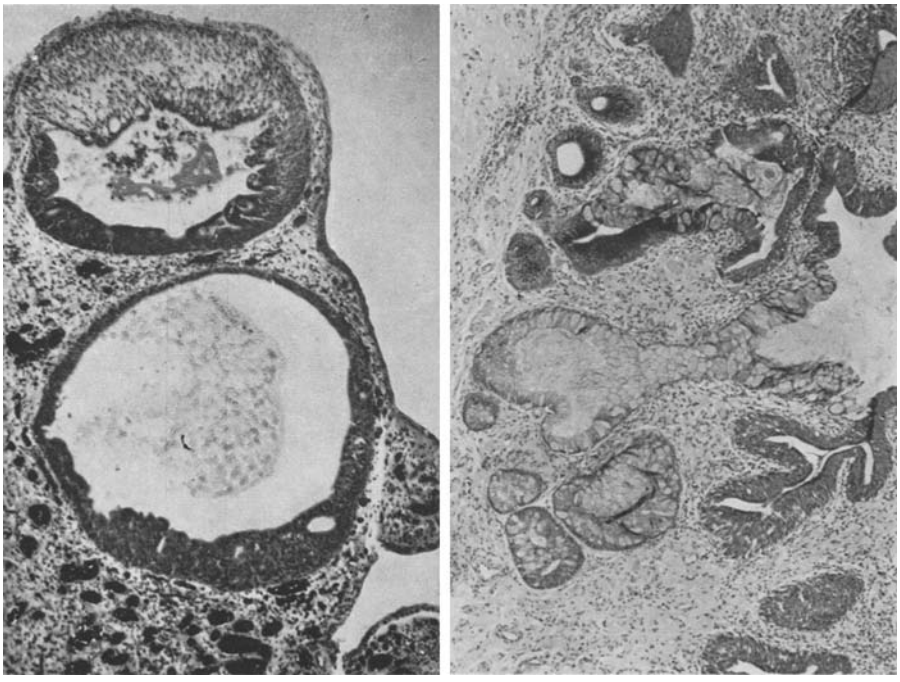

Fig. 5. a Case V, Cystitis cystica bordering an area of acute inflammation in *Esch. coli* cystitis. H. & E., mag. × 40. b Case IV, Cystitis glandularis in *Esch. coli* cystitis. Abrupt transition between normal urothelium and mucus secreting epithelium. PAS, mag. × 45

The clinical corollary of this is that a kidney which is nonfunctional because of stone and pyonephrosis should be removed, and the metaplastic epithelium of the renal pelvis regarded as, at least potentially, premalignant.

Glandular Metaplasia and Infection

In a series of experiments designed to define the lesions of pyelonephritis, de Navasquez (1950) injected suspensions of Staphylococci intravenously into rabbits. In one rabbit, the longest survivor of the test animals, he found glandular metaplasia of the renal collecting tubules and pelvis. All the cases of pyelitis glandularis, and almost all the cases of adenocarcinoma of the renal pelvis in the literature are associated with pyonephrosis or pyelonephritis, and Pugh (1959) noted that mucus secreting epithelium occasionally marginated the areas of inflammation and ulceration in *Esch. coli* cystitis (Cases IV and V).

Stoerck (1899) gave the first illustrated description of cystitis glandularis and established its relationship with adenocarcinoma of the bladder. In a later paper (1911) he showed its relationship to infection, and emphasised the common reaction of the epithelial lining of the renal pelvis, ureter, bladder and prostatic urethra. Many other authors (Morse, 1928; Stirling, 1942) have since described pyelitis, ureteritis and cystitis cystica and further emphasised the relationship with infection, but glandular metaplasia of the intestinal type remains uncommon

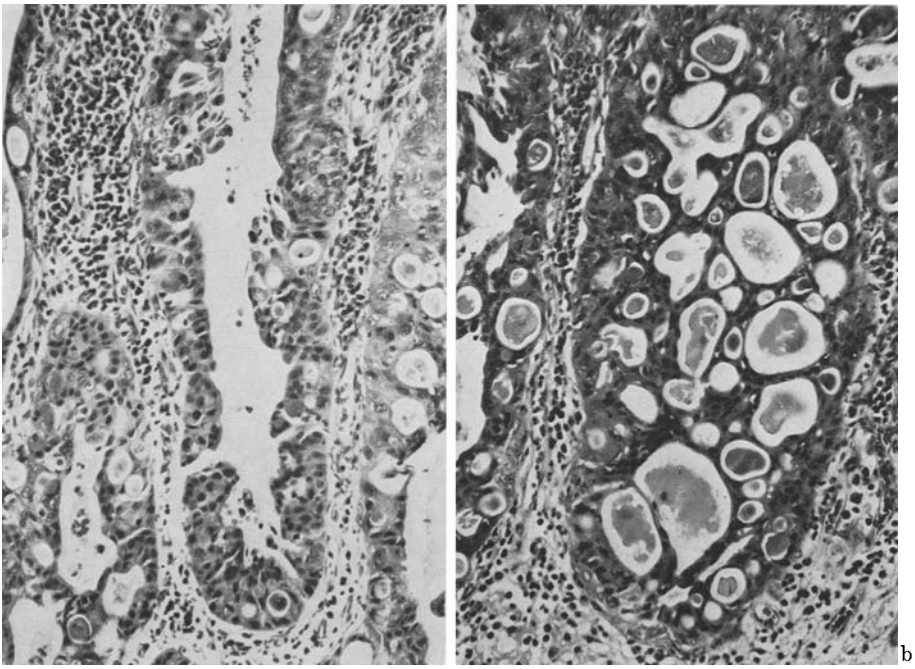

Fig. 6. a Case VII, Pseudoglandular pattern in a transitional cell carcinoma. The proteinaceous material in the glandlike spaces is PAS and mucicarmine positive. H. & E., mag. × 100. b Case VII, Pseudoglandular pattern in a transitional cell carcinoma. H. & E., mag. × 100

(Parker, 1970). Giani (1906) produced a similar lesion in rabbits with experimental cystitis; and Langham *et al.* (1944) described papillary adenomata in two Guernsey cows that were discovered during a survey of pyelonephritis in cattle.

Makar (1957, 1962) noted that cystitis cystica and cystitis glandularis were relatively common in vesical bilharzia (Case VI, Fig. 8) but that adenocarcinoma was unusual, the majority of malignancies in the bilharzial bladder being squamous carcinomas. Makar and Urquhart (1930) described a case of fairly extensive cystitis glandularis in a 40 year old fellah but saw no evidence of active bilharzia in the lesion, and attributed the glandular appearances to foetal rests. Urquhart (1931) described cystic changes in the ureter in bilharzia, but again true glandular metaplasia was not present. There is one recent documented case of adenocarcinoma associated with bilharzia (Sayegh and Ishak, 1957) but that is in a case of exstrophy and cannot be attributed to the bilharzia alone. Goebel (1905) discussed 20 cases of carcinoma of the bladder in bilharzia, 11 of which were squamous carcinoma, and 1 an adenocarcinoma, but give no clinical details. Fergusson (1911) described a further 40 cases, all of which were squamous carcinoma. Harrison (1889) described the first case of adenocarcinoma of the bladder that can truly be attributed to bilharzial infection. Dimmette *et al.* (1956) described 6 adenocarcinomas in 90 cases of vesical bilharzia and carcinoma, Aboul Nasr *et al.* (1962) 14 in 300, Higginson and Oettle (1962) 1 in 23, and Dodge (1962) 5 in 76—an overall incidence of 4–5%, although Gillman and

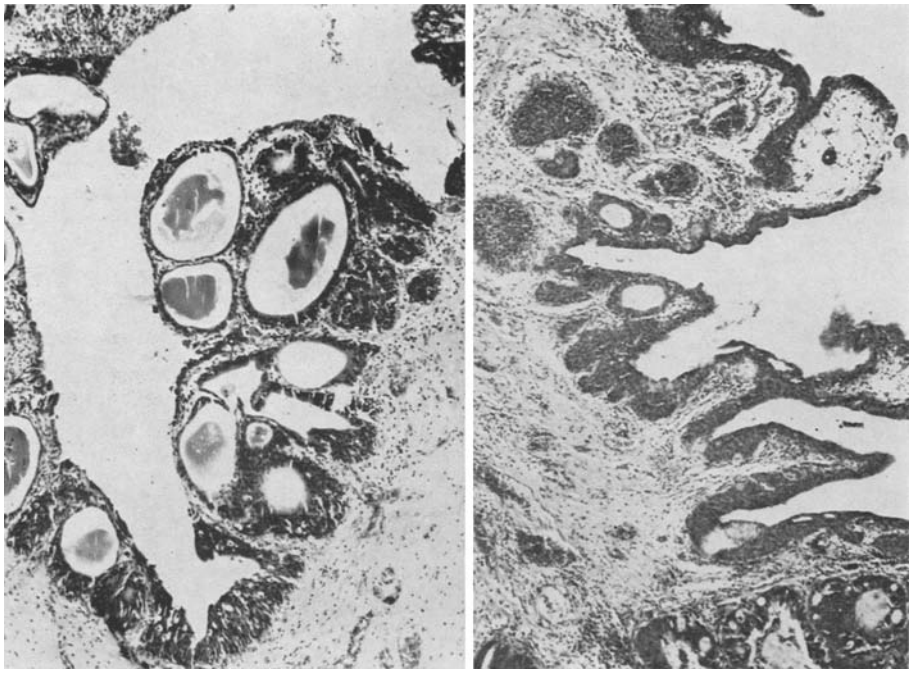

Fig. 7. a Case VIII, Cystitis cystica bordering a carcinoma of urachus. H. & E., mag. × 45. b Case IX, Cystitis cystica and epithelial rests bordering a metastatic carcinoma of rectal origin. H. & E., mag. × 35

Prates (1962) failed to find cystitis glandularis or adenocarcinoma in a series of cases from Portuguese East Africa.

Glandular Metaplasia and the Absence of Urine

Aiken (1955) made the ingenious suggestion that the absence of urine prompted the urothelium to undergo intestinal type metaplasia. Although this theory cannot provide the sole cause in all cases, and cannot explain many of the vesical cases of adenocarcinoma, it could well be a contributory factor. The majority of urachal tumours are mucoid adenocarcinoma, and although the normal urachal epithelium is urothelial in type, it *is not usually in contact with urine.* Glandular metaplasia, and adenocarcinoma, are common in the exstrophic bladder, occurring initially on the superior and lateral aspects. The urine flow lubricates the central and inferior parts of the defect, leaving the *superior and lateral parts free of urine contact.* Gordon (1963) provided further evidence in support of this theory, although he made no mention of it at the time. He described a male aged 50 years with spina bifida, who had had a suprapubic cystotomy and bilateral ureterocolic anastomoses performed in adolescence for bladder dysfunction. He subsequently developed pyonephrosis, and an adenocarcinoma of the renal pelvis. The afunctional bladder showed cystitis glandularis with Paneth cell differentiation, that is to say, complete intestinal-type metaplasia.

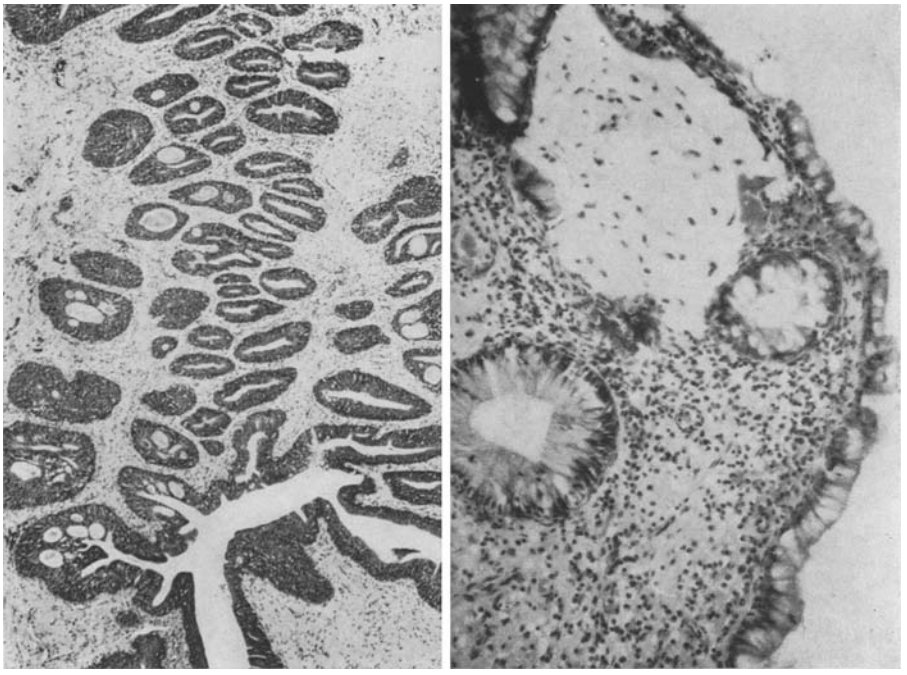

Fig. 8. a Case VI, Cystitis cystica in vesical schistosomiasis. H. & E., mag. × 35. b Case VI, Cystitis glandularis in vesical schistosomiasis. H. & E., mag. × 95

Glandular Metaplasia in Relation to Tumours

Cystitis cystica is a reactive phenomenon of the urothelium and, as such, may be seen in relation to neoplasms within or under the mucosa (Cases VIII and IX). Stoerck (1899) described cystitis cystica and glandularis in relation to a metastatic carcinoma in the bladder (Case IX, Fig. 7 b), and Stanley and Dockerty (1965) described cystitis cystica in relation to vesical endometriosis. Wheeler and Hill (1954), Mostofi *et al.* (1955) and Grogono and Shepheard (1969) make the assertion that urachal adenocarcinoma can only be diagnosed, among other factors, in the absence of cystitis cystica and cystitis glandularis in the adjacent mucosa. This does not, however, always hold good, and cystitis cystica *may* be seen in relation to urachal adenocarcinomas (Case VIII, Fig. 7 a), as might be expected in view of the relationship of proliferative urothelial lesions to metastatic tumours and endometriosis. Melicow (1952) showed cystitis cystica and cystitis glandularis in grossly normal mucosa adjacent to transitional cell carcinomas of the bladder. Salm (1967) considered cystitis cystica in this situation to be a field change in response to the neoplastic stimulus, and Schade and Swinney (1969) claimed to have found cystitis glandularis in 20% of biopsies taken from "normal" mucosa adjacent to transitional cell carcinomas, although their illustrations show only cystitis cystica.

Parasitic Origin for Cystitis Cystica

Eve (1889) described ovoid bodies amidst the colloid content of cystitis cystica and attributed these to the cysts of a parasite—*Psorospermia*. Many authors, notably Bland Sutton (1889) Clark (1892) and Voelcker (1898), supported this theory with similar observations and it remained current until about 1920. Despite extensive search, no vegetative parasites were discovered and the theory was eventually discarded. Giani (1907) illustrates a similar picture to that described by Eve, and identifies the bodies as desquamated epithelial cells. A similar appearance is also seen in Case III where the ureteritis cystica shows discrete colloid globules amongst the cyst contents (Fig. 2d).

Enteric Rest Theory for Cystitis Glandularis

Hache (1888) proposed enteric rests as the origin of glandular tissue in the bladder, particularly the exstrophic bladder. This theory was taken up and expanded by Lecène and Hovelacque (1912) and Francois (1913) to include cystitis cystica as well as cystitis glandularis and adenocarcinoma. Later Colby (1925) noted cystitis glandularis in the trigone and likened the appearances to the mucosal changes in exstrophy, attributing both to embryonic rests. Various other authors followed this line of argument, but the theory has now been generally discarded in favour of one of metaplasia.

Glandular Neoplasia in Animals

Spontaneous bladder tumours in animals are rare. Willis (1960) referred to tumours of the bladder in horses, cattle and dogs; Pamukcu (1962) described vesical tumours in cattle and water buffalo; Rewell and Willis (1950) described a vesical papilloma in a mongoose and a squamous carcinoma in a fishing cat; and Cotchin (1959) reported a series of 22 carcinomas of the bladder in dogs. The squamous carcinoma in the fishing cat (Rewell and Willis, 1950) did show a pronounced pseudoglandular pattern; and Cotchin (1959) described, and illustrated, a pseudo-adenomatous growth pattern in transitional cell carcinomas of the bladder in dogs, with the formation of false tubules and the collection of an apparent secretion within the lumen. This feature is seen in Case VII (Fig. 6). Feldman (1930) and Langham *et al.* (1944) describe cases of what they called adenomata of the bladder in cattle. The histologic description and illustrations are similar to the appearances in polypoid cystitis glandularis (Case IV); and in one case (Langham *et al.*, 1944) the glandular epithelium appears to be bordering on carcinomatous change. Pamukcu (1962) illustrated two cases of adenocarcinoma occurring in cattle and noted a number of other cases in association with mesodermal vesical lesions. He also showed that other vesical epithelial neoplasms could undergo metaplastic change to give a pseudoglandular appearance. In an extensive discussion of the subject, he considered that vesical adenocarcinoma in cattle was metaplastic in origin and arose from the transitional epithelium rather than from embryonic rests. Mugera *et al.* (1969) mention both adenomas and adenocarcinomas as occurring in Kenya Zebu cattle, and also illustrate adenomatous change in transitional cell lesions.

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