THE SURGICAL SEQUELAE OF BILHARZIAL DISEASE*

CHARLES MARKS, M.B., CH.B., M.R.C.P., F.R.C.S.
Salisbury, S. Rhodesia

Introductory: For a great many years authorities have been preoccupied with the epidemiological and preventative aspects of this almost universal scourge of the African continent. Undoubtedly the prophylactic measures aimed at killing all snails in the watercourses of the affected areas, and the early diagnosis and treatment of human victims, are of the greatest importance in containing this common disease. With an infestation rate of 80% amongst the Africans and 10% amongst the Europeans in the Central African Federation a sure knowledge of the natural history of schistosomiasis is essential, for in the course of years there occurs a degree of destruction and interference with the function of organs which makes the role of reparative and reconstructive surgery in this disease of great importance. I became aware of these facts soon after commencing surgical practice in Salisbury and it is on the basis of my observations in this regard that I have prepared this paper.

Though Pruner was the first accurately to describe the clinical features of vesical schistosomiasis, the etiological agent was not discovered until 4 years later, when Theodor Bilharz, in 1851, discovered a trematode worm in the portal vein of a patient, naming it the *Distoma haematobium*. Bilharz further correlated the relationship between this trematode and the symptoms of haematuria and diarrhoea which resulted from involvement of the bladder and large bowel respectively, whilst it remained for Leiper to work out the life history of the worm and to demonstrate that the urinary and intestinal forms were caused by infestation with two distinct species of schistosoma viz. *haematobium* and *mansoni* respectively. The work of Leiper, Manson-Bahr and Fairley proved that the fresh-water snail acted as the intermediate host; *Physopsis africana* (genus *Bulinus*) for *Schistosoma haematobium*, and *Biomphalaria pfeifferi* (genus *Planorbis*) for *S. mansoni*.

Bilharzial infestation affects vast tracts of the African continent extending in a wide belt along the Nile River into the Sudan, then along the East Coast, including Eritrea and Somaliland, Uganda, Kenya and Tanganyika. It affects the territories of the Central African Federation and the Eastern half of the Union of South Africa (Eastern Transvaal and Natal), extending to the Cape on the East Coast. Portions of French West Africa, Sierra Leone and the Gold Coast are also affected. Bilharziasis also occurs in Japan, China and the Phillippines (*S. japonicum*) as well as in South America and the West Indies, so that if one accepts the global nature of modern medicine and surgery this becomes a disease of great importance as well as great interest.

NATURAL HISTORY

The sexually-distinct digenetic trematodes of the genus *Schistosoma* inhabits the portal system of the human victim of this disease. The 11-mm.-long male worm is shorter and broader than the female of the species and widens just caudally to the ventral suckers to form a gynaecophoric canal, within which the female is enclosed in times of sexual activity. The lateral-spined ova of *S. mansoni* are deposited mainly in the colon and rectum, whilst the terminal-spined ova of *S. haematobium* reach the vesical plexus and are deposited in the bladder and lower ureter, initiating the pathological changes which in the course of time may require surgical attention.

Many eggs, however, are voided in the urine and faeces, perpetuation of the life cycle becoming contingent upon their reaching the appropriate fresh-water snail within 24 hours. Osmotic pressure effects cause disintegration of the ova's chitinous shell, with release of its contained miracidium, which penetrates the snail's antennae and, reaching the snail's subcutaneous tissues, develops through the sporocyst stages into the bifid-tailed larval cercariae. The cercariae bore their way through the snail's soft tissues and are ejected in puffs from the snail's pulmonary system into the surrounding water.

The cercariae possess, in primitive form, all the adult appendages and, coming into contact with the skin or mucous membrane of man, they pierce their way to the lymphatics, provoking at their sites of entrance small reddish-brown papules known as 'swimmer's itch'. Reaching the venous system the trematodes travel to the right heart and thence *via* the pulmonary circulation to the lungs. Returning to the left heart they are then dispersed *via* the aorta to the gastro-intestinal tract, returning to the portal vein, from where they commence their retrograde sojourn along either the superior or inferior mesenteric vein, thus reaching their urinary and intestinal destinations.

During this migratory period, systemic disturbances are not uncommon. General ill-health, malaise and proneness to fatigue may be manifest, whilst recurrent bouts of pyrexia of uncertain origin may cause diagnostic difficulty. Urticaria, transient pulmonary infiltrations and generalized lymphadenopathy are not unusual features, whilst haematological investigations may disclose a normochromic anaemia associated with an eosinophilia of 10-60%.

THE URINARY SYSTEM

The Bladder

The urinary tract is peculiarly susceptible to oviposition by *S. haematobium*. After the migration of the coupled worms to the vesical venous system the female deposits her eggs in the terminal venues, the ova advancing to the submucous layer of the bladder. Acting as a vesical irritant, the ovum sets up a local inflammatory reaction, which may be visualized cystoscopically early in the disease, at a stage when microscopic examination of the urine will show it to be teeming with terminal-spined ova and red cells. Cystoscopic examination at this stage

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discloses an intense hyperaemia and oedema of the peri-ureteric vesical mucosa. In the course of the next 6 weeks grayish-yellow tubercles will be visualized on the trigone and around the ureteric orifices, a fine zone of hyperaemia being discernible around the tubercles. Urinary microscopy at this stage may fail to reveal ova, but cystoscopic biopsy of pathological foci readily affords histological confirmation of the diagnosis.

Blockage of the submucous glands in association with the inflammatory reaction results in the formation of pale bullous cysts, which are seen at cystoscopy to be arranged focally or in clusters. Occasionally one has seen an appearance not unlike cystitis cystica. Cystoscopic control during systemic antimony therapy permits assessment of the local response to treatment, and permits assurance that the lesions are reversible. After completion of treatment the affected vesical mucosa bears a permanent golden-yellow punctate appearance.

With progression of vesical changes, the epithelium becomes heaped up into papillary projections by the vascular inflammatory granulation-tissue which develops. These changes are in keeping with changes, demonstrated by Rolnick (1949), that occur when the vesical mucous membrane is exposed to irritation. It is, in my opinion, wrong to refer to these masses as papillomata, which implies that they are neoplastic in nature, the true papilloma being notorious for its malignant propensities and for its ability to give rise to seedling growths even when histologically benign. These masses respond extremely well to a combination of systemic therapy and local cystoscopic fulguration, leaving small fibrotic nodules as the sole evidence of their past existence. I would therefore suggest that these masses be referred to as papillary bilharziomas, a term that adequately describes their inflammatory nature.

Ulceration of the bladder, though not common, may occur, and a vesico-vaginal fistula may follow. Rupture of the bladder may take place at the site of bilharzial ulceration, and it is as well to remember that malignant vesical ulceration may be associated with bilharzial cystitis; hence the necessity for histological study of a biopsy specimen before systemic antimony therapy is begun. Secondary infection may result in a focal or general phsophatic incrustation of the bladder mucosa.

It is not without some interest to refer to the rarity of urinary lithiasis in the African despite the frequency of gross structural changes. Thus amongst 66,842 Bantu admissions only 14 cases of calculus disease were discovered (10 vesical, 2 urethral, 1 renal and 1 ureteric). During the same period of time 84 cases of urinary lithiasis occurred amongst 28,547 European hospital admissions. Undoubtedly urinary stagnation is less important than the low dietary calcium and acid ash-residue of the African's diet, in the pathogenesis of urinary lithiasis.

Extremely striking is the frequency of vesical, and occasionally ureteric, calcification which follows heavy bilharzial infestation. The calcification is arranged concentrically, providing a marked resemblance to the radiological appearance of a foetal head *in utero*.

Diminution of the bladder capacity will give rise to back-pressure effects, with varying degrees of mega-ureter and hydronephrosis, but it is often a source of surprise to find that, despite gross organic structural changes, physiological reserves are such that function is not too greatly disturbed.

It has long been held, on rather indefinite evidence, that there is a close etiological relationship between bilharzial infestation and carcinogenesis. Since Ferguson in 1911 published his observations on a series of 40 cases of vesical bilharziasis associated with primary malignant disease of the bladder, it has been continually imputed that the irritative effects of the trematodal ova together with the effects of long-standing sepsis exert a focal carcinogenic effect. In an attempt to assess this problem in the light of experience in Salisbury I have analysed the incidence of primary vesical carcinoma in European and Bantu. In 28,547 European hospital admissions 20 cases of bladder cancer (0·07%) were seen, whilst during the same period of time 66,842 African admissions provided 78 cases of vesical carcinoma (0·12%). Analysis of the 78 cases of vesical carcinoma demonstrated that in 43 of these cases was there concomitant bilharzial cystitis, vesical calcification or histological evidence of oviposition. In view of the fact that 80% of the African population suffers bilharzial infestation no statistical significance can be attached to the occasional (56·4%) association of both diseases. Moreover, the incidence of bladder cancer in this bilharzial region is no greater than that in non-bilharzial areas (Flocks 1946, Milner 1946, Marshall and Whitemore 1951).

It would also be anticipated that if bilharzial cystitis played a part in focal carcinogenesis, it would do so by causing an epithelial metaplasia and thus produce a squamous-cell carcinoma. The commonest type of vesical cancer encountered in those cases where bilharzia and cancer co-exist is a proliferative carcinoma of transitional or mixed-cell type, whilst the maximal proliferation is found at sites where the ova exist in least concentration. Nevertheless it is a fact that carcinoma occurring in a bilharzial bladder spreads more readily to adjacent organs and structures.

The Ureter

It has been indicated above that the earliest vesical involvement occurs in the peri-ureteric region. It is therefore logical to anticipate that cicatrization and fibrosis at the ureteric orifice should occur, resulting in stricture and obliteration of that orifice. The traction effects of peri-ureteric fibrous tissue may, and often do, result in a gaping 'golf-hole' ureteric orifice not unlike that of tuberculosis. The resultant incompetence of the ureterovesical mechanism permits reflux of urine up the ureter and, augmented by superposed recurrent sepsis in the ureter and kidney, gives rise to one form of bilharzial mega-ureter and hydronephrosis.

The pelvic ureter often suffers oviposition and the subsequent pathological changes will determine whether ureteric stricture, ureterectasia, or ureteric calcification will follow. By ureterectasia I refer to a primary focal dilatation in the lower ureter, unassociated with distal obstruction or uretero-vesical incompetence. It is due to the constant stress imposed by the propulsion of urine

on an area weakend by fibrous tissue-replacement of the destroyed contractile muscle layer. This localized dilatation results in varying degrees of neuro-muscular incoordination in the ureteric propulsive effort and progressive dilatation occurs in a cephalad direction.

Bilharzial mega-ureter may thus follow ureteric stricture localized to the orifice or to the pelvic ureter; it may follow ureterectasia and ureteric calcification; it may result from uretero-vesical incompetence; or it may follow back-pressure from a small-capacity bladder.

Without wishing to discourse at length on the indications for surgical treatment in the sequelae of bilharzial disease, I would like to mention a few of the procedures which may provide great relief:

Cystoscopic meatotomy of the stenosed or cicatrized ureteric orifice, followed by regular bougie dilatation, may confer great benefit on the patient, whilst ureteric bouginage often controls stricture of the lower ureter and prevents back-pressure effects. Bouginage, however, is useless in ureterectasia, so that an early decision should be made to resect this segment of ureter if recurrent sepsis or back-pressure effects ensue. Similarly ureteric resection is carried out if a stricture is impassable or repeated dilatations prove ineffectual. After resection of several inches of lower ureter it has always been found possible to perform a uretero-cystoneostomy, but if excessive tension prevents anastomosis it is possible to bridge the gap with a length of ileum. Transplantation of the ureters into the pelvic colon would be indicated if a completely disorganized bladder with internal or external fistula existed, whilst ileocystoplasty may permit an increase in bladder capacity where this is desirable. Nephrectomy or nephro-ureterectomy may have to be performed on its merits but one must be absolutely certain that the contralateral kidney is not heir to progressive damage, whilst nephrostomy or pyelostomy may be a necessary preliminary manoeuvre before excision of the distal ureter can be considered.

THE ALIMENTARY SYSTEM

S. mansoni has a special predilection for that part of the alimentary tract which is drained by the inferior mesenteric vein. Bilharzial colitis and proctitis gives rise to abdominal pain and periodic bouts of diarrhoea with blood and mucus in the stools. The ova may be found in the stools, but sigmoidoscopy is often desirable. The earliest change visualized through the sigmoidoscope is a congested haemorrhagic mucosa, and biopsy of the rectal mucosa readily affords histological confirmation of the disease. The development of a large rectal bilharzioma may cause confusion with carcinoma, but biopsy will readily differentiate between the two, and in passing it can be definitely asserted that rectal or colonic bilharziasis is never potentially malignant; it resolves rapidly with systemic antimony therapy.

Perianal or perineal bilharzial granulomata may occasionally be the presenting lesion, resolving rapidly with antimony therapy.

The vermiform appendix is one of the organs very susceptible to oviposition, but it is interesting to note that in 92% of cases of appendiceal bilharziasis *S. haematobium* is the cause. Thus the association of urinary and appendiceal bilharziasis is a common one and should be borne in mind when symptoms indicate a mixed urinary and appendicular pattern. It is, however, as well to appreciate that the relationship between the appendix and bilharzial infestation may take two forms:

1. Appendiceal bilharziasis: Oviposition occurs in the appendix, undergoes healing without involvement of the lumen and does not cause clinical disturbance, being a fortuitous finding.

2. Bilharzial Appendicitis: As a result of gross structural change, with partial or total obliteration of the lumen, features of chronic appendicitis result, whilst in a proportion of cases it predisposes to acute and subacute pyogenic appendicitis. Occasionally the appendix is incorporated in a large bilharzial granulomatous mass.

Bilharzial hepato-splenomegaly

The intimate relationship between the liver and spleen on the one hand, and the portal circulation on the other, adequately explains the frequent presence of schistosomal ova in the liver (56%) and to a lesser extent in the spleen (10%) noted by Gelfand (1950) in his autopsy series.

Oviposition in the liver causes a local inflammatory reaction resulting in the formation of multiple tubercles. Only occasionally do tubercles coalesce to form a large hepatic bilharzioma, whilst on rare occasions secondary infection will result in the formation of a liver abscess.

The term Egyptian splenomegaly is synonymous with bilharzial splenomegaly, yet only rarely are ova found in the Egyptian spleens, it being suggested that bilharzial toxins or bilharzial chronic pancreatitis acts as the cause. If one accepts that the syndrome falls into the group now referred to as portal hypertension, then it is probable that the main cause is a trophopathic lobular cirrhosis due to subnutrition, the concomitant bilharzial infestation not playing a great part in its etiology. The possibility that obstruction of the portal veins by the trematode, or by trematodally induced thrombosis, is a factor that has been investigated fruitlessly.

MISCELLANEOUS SURGICAL LESIONS

Bilharzial salpingitis, cervicitis and vaginitis are often encountered and undoubtedly play a role in the causation of sterility and ectopic pregnancy. The presence of bilharzial ova in the uterus and in the centre of uterine fibroids also raise points of interest.

It is interesting to note that only rarely are the male genital organs clinically involved by bilharziasis though the occasional case of bilharzial orchitis does occur, making its consideration in the differential diagnosis of testicular swellings necessary. Though bilharzial tubercles are often noted in the tunica vaginalis it is not a factor in the causation of hydrocoele.

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