Summary

Investigation of haemodynamic changes in schistosomal cor pulmonale showed:

(A) The presence of broncho-pulmonary arterial shunts proved by: (1) absence of correlation between the size of the pulmonary artery and its luminal pressure; (2) a progressive increase in the oxygen saturation in the pulmonary artery along its course; (3) the appearance in the pulmonary artery in $1\frac{1}{2}$ seconds of Evans blue dye injected into the aorta; (4) a sudden increase in the pressure as the catheter was drawn from the wedge to the pre-wedge position; and (5) on aortography by a special technique, the rapid filling of the

big branches of the pulmonary artery through the bronchial arteries.

(B) The presence of splenic shunts, as evidenced by: (1) a fall in the oxygen saturation in the inferior vena cava after splenectomy; and (2) a change towards normal in the size of the heart, in the electrocardiogram, and in the pulmonary arterial pressure after splenectomy.

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SCHISTOSOMIASIS OF THE CERVIX

BY

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Although schistosomiasis usually involves the urinary tract and the rectum, schistosomiasis of the genital tract is not infrequently encountered in areas heavily infested with the disease. The disease may be discovered during examination of patients for other gynaecological conditions or it may itself produce symptoms that will bring the patient for examination. Schistosomiasis may affect any component of the female genital tract, the site of predilection of the infestation differing in different countries according to the infesting species. Thus in countries in which the common species of the worm is *Schistosoma mansoni* the Fallopian tubes and the ovaries are the organs usually involved (Areal, 1956). In Egypt, where *S. haematobium* is more prevalent, we find that the lower components of the genital tract—namely, the cervix, vagina, and vulva—are the organs more often involved. Moreover, gynaecological manifestations as a whole are more common with the *S. haematobium* than with *S. mansoni* infections.

The importance of schistosomiasis of the cervix is twofold: it may be mistaken for carcinoma and it may possibly, though rarely, predispose to that disease.

The present article is based on cases personally encountered in the years 1950–60 inclusive, together with a study of biopsy material of schistosomiasis of the cervix in the Kasr el Aini Hospital during that period.

Four cases of peculiar interest are reported: in one case carcinoma of the cervix developed on the top of schistosomiasis of the organ; in another a schistosomal papilloma concomitant with pregnancy simulated carcinoma, the pregnancy itself terminating in abortion; in the third case the disease has caused marked hypertrophy of the cervix; and in the fourth case the presence of schistosomiasis has predisposed to a ureteric fistula after labour.

Material

During 1950–60 88 cases of schistosomiasis of the female genital tract were seen. The distribution of the lesions among the various components of the genital tract is shown in Table I, and the age incidence in Table II.

Schistosomiasis of the vulva was encountered at an earlier age (most of the patients were in the age-groups 11–30 years) than schistosomiasis of the cervix (the majority in the 21–40 year group). One probable reason

is the fact that vulval lesions are noticed by the patients at an earlier age. Nevertheless from this study it is felt that when schistosomiasis of the genital tract affects a woman of over 35 years the cervix is the site of predilection, while if it affects a young girl it occurs in the vulva with greater frequency.

TABLE I.—Organs Involved in 88 Cases

Vulva	9 cases	Corpus uteri	5 cases
Vagina	25 "	Fallopian tube	7 "
Cervix	32 "	Ovary	4 "
Cervix and vagina	2 "	Peritoneum and broad ligament	2 "
Urethra	2 "		

TABLE II

Age	No. of Cases of Schistosomiasis of Cervix	No. of Cases of Schistosomiasis of Vulva
0–10	1	1
11–20	2	5
21–30	14	3
31–40	13	0
41–50	4	0
51–60	0	0
Total	34	9

The macroscopical appearance of the lesion in the 32 cases of cervical schistosomiasis is described in Table III.

TABLE III.—Gross Appearances of Lesion in 32 Cases of Schistosomiasis of Cervix

Schistosomal papillomata	11 cases
Nodular and diffuse hypertrophic cervix	15 "
Erosion of cervix with or without sandy spots	3 "
Carcinoma	3 "

There were three cases of carcinoma of the cervix superimposed on schistosomal affection. All the three were of the squamous-cell type. There was also a case of papillary cystadenocarcinoma superimposed on schistosomiasis of the ovary.

Case 1

A woman aged 28 was admitted to Kasr el Aini Hospital on May 24, 1959, complaining of offensive yellowish vaginal discharge since her last delivery, four months before admission. She had had four pregnancies; the first three were full-term normal labours and the last was a premature labour of 28 weeks, the child dying four hours after delivery. Menstruation reappeared two months after delivery and had been regular since then, 5/28 days. The last menstrual period ended three days before admission.

On examination her general condition was fair. The chest and heart were free. On vaginal examination the

uterus was of normal size and retroflexed. The cervix was hypertrophied, nodular, and indurated. There was an ulcer on the anterior lip; the ulcer had a friable edge. The fornices were the seat of hard nodules. Cystoscopy revealed schistosomal sandy patches in the trigone. A punch biopsy from the edge of the ulcer revealed the presence of a fairly well differentiated carcinoma. There were schistosoma ova in between the cell buds. The epithelium at the edge of

FIG. 1.—Case 1. A schistosoma ovum amid cancer cells. ($\times 450$.)

FIG. 2.—Case 2. Schistosoma cervical polyp with pregnancy.

sessile, 2 cm. in diameter, congested, and had an ulcerated and bleeding surface. There was no bleeding from the external os. A punch biopsy was made from the mass. One week after admission the bleeding became more severe and the patient felt intermittent colic. On examination the cervix was found dilated and there was mild bleeding from the external cervical os. A few hours later abortion occurred. Two weeks after the abortion the mass became pedunculated, its surface became healthy, and there was no bleeding. A course of tartar emetic was given and the polyp was excised.

Biopsy.—The polyp was covered by squamous epithelium showing marked keratinization, acanthosis, and parakeratosis. Underneath the epithelium were many schistosoma ova with marked vascularity of the tissues around them (Fig. 2).

Case 3

A woman aged 38 and married for 20 years was admitted to Kasr el Aini Hospital on September 20, 1949, for

the cancer showed excessive cornification, parakeratosis, and acanthosis (Fig. 1).

A Wertheim operation was performed, being followed by a course of x-ray therapy. She left hospital in good condition after completion of radiotherapy, three months after the operation.

Case 2

A married woman aged 31, a para-2, was admitted to Kasr el Aini Hospital on January 12, 1960, complaining of mild vaginal bleeding of 20 days' duration. Her last menstrual period was nine weeks before admission and she had breast enlargement and morning sickness.

On examination she was anaemic; the uterus was enlarged and soft, its size corresponding to the period of a menorrhoea. There was a mass on the cervix, 1 cm. to the left of the internal os. The mass was

excessive mucopurulent discharge and bleeding during coitus. She had had seven full-term labours and one abortion at three months. Her menstrual periods were regular, 5/29 days. Her general condition was good. On vaginal examination the cervix was remarkably hypertrophied, with an irregular granular surface. Owing to the

FIG. 3.—Case 3. A male and a female schistosoma worm seen together in a vein. ($\times 100$.)

FIG. 4.—Case 3. Marked epithelial hyperplasia associated with schistosomiasis of the cervix. ($\times 35$.)

unhealthy appearance of the cervix, a biopsy was made. One week later partial amputation of the cervix was performed.

Biopsy.—The amputated cervix was heavily infested with schistosoma ova and worms. The cervical epithelium was very hyperplastic, but there was no evidence of cancer (Figs. 3 and 4).

Case 4

A married woman aged 26, a para-1, was admitted to Kasr el Aini Hospital with a urinary fistula which had appeared 10 days after a prolonged (three days) but spontaneous delivery.

On vaginal examination the cervix was of normal size but was the seat of a concentric flat erosion. Scattered over the surface of the erosion were tiny white spots each

the size of a pinhead. There was slight bleeding on contact. Urine was dribbling from a fistulous orifice situated in the right fornix. The orifice was red in colour, and 4 mm. in diameter. Pouting from the orifice were red granulations, and scattered over the latter were white spots similar to those over the cervical erosion. The fistula proved by cystoscopy and by the methylene blue test to be a right ureteric lesion. A punch biopsy from the cervix and from the red granulations surrounding the ureteric fistula showed multiple schistosomes. A course of tartar emetic followed by a uretero-vesical implantation operation cured the incontinence and the schistosomal lesion in the cervix.

Discussion

It is not necessary to go into any detail about the life history of schistosome. The organism is a bisexual trematode and the male and the female live in the portal vein and its tributaries. The male worm is about 10 mm. in length and 2 mm. in breadth, has a flat body, and, because of its mammillated surface and two suckers it can anchor itself to the venous wall. The body is folded upon itself forming a gutter, the gynaecophoric canal which lodges the female worm. The latter is twice as long as the male and, unlike it, its body is rounded and much narrower. There are three species of the worm—*S. haematobium*, *S. mansoni*, and *S. japonicum*. The worms leave their normal habitation and swim against the venous current, the male taking the female within its fold, passing to the haemorrhoidal veins and then through anastomotic veins into the vesical venous plexus if the worms belong to the species *S. haematobium*. *S. mansoni* worms settle in the venules of the colon and rectum. The worms, of whatever species, progress along the venule until the male by its bulk cannot go any further. The female then leaves the male and proceeds into the small tributaries of the vein until it cannot progress any further. The venule is thus plugged by the female worm, and there the female lays its eggs. The female then retreats and rejoins the male. The ova are extruded in the urine and the stools by contraction of the bladder and the rectum respectively. If the ova are deposited by chance in fresh water they hatch out their miracidia, which swim actively searching for their intermediate host, which is a snail. The miracidium undergoes a series of changes in the snail until it is discharged eventually from it as cercariae which have bifurcated tails. These search for their definitive host—man—pierce the human skin, and pass into the circulation. Only those that reach the portal vein live and grow.

Schistosomal Reaction in the Cervix

The deposition of schistosome ova in the small venules of the cervix causes an inflammatory reaction in the tissues around them together with marked hyperplastic changes in the covering epithelium. The changes are more pronounced in the squamous epithelium covering the portio than the columnar epithelium lining the cervical canal. Consequently it is convenient to discuss the changes in the cervix under two headings: (1) the changes in the submucous tissues and (2) the changes in the cervical epithelium.

Changes in Submucous Tissues.—The presence of ova each enclosing a miracidium excites a fibrocellular reaction in the tissues around them. Thus we find the ovum surrounded by a big giant cell which in turn is surrounded by epithelioid cells, and the latter are also surrounded by eosinophils and lymphocytes. This is

the unit schistosomal lesion or the schistosomal turnover which resembles the tuberculoma but differs from it by the presence of caseation and the presence of schistosome ova in the former. Later fibrosis takes place with gradual disappearance of the cellular components. This causes hardness and puckering of the cervical tissues.

Changes in Cervical Epithelium.—These changes are most pronounced in the squamous epithelium covering the portio vaginalis. The cervical epithelium increases in thickness, perhaps four to five times its normal thickness. There is a well-marked keratin layer over the surface. Parakeratosis is also a prominent feature. At the same time flask-like downgrowths penetrate into the submucous layer. The basal layer is often multilayered and its cells stain more deeply than normal. Islands of epithelium are often found separated from the surface. These epithelial changes are similar to the changes that take place in leucoplakia; in fact, leucoplakia areas, both gross and microscopic, are frequently encountered.

When fibrosis sets in it may lead to obstruction of the necks of the cervical glands and they then become dilated.

Gross Appearance of the Schistosomal Cervix

As a result of the hyperplastic changes in the epithelium and the inflammatory reaction in the submucous tissues cervical schistosomiasis may present itself in one or more of the following pictures.

Schistosomal Sandy Spots.—These are not seen by the naked eye in a cervix covered by squamous epithelium, but they are apparent if they happen to lie underneath an erosion. They looked like tiny dots similar to white grains of sand, and each is the size of a pinhead. Microscopical examination shows that each grain is schistosomal. They do not appear under the squamous epithelium thick as it is in schistosomiasis.

Diffuse Schistosomal Infiltration.—The cervix is swollen and firm, has a granular surface, and may be ulcerated in some areas. The epithelium overlying it may be thrown into villus-like folds or may have a mulberry surface. Near the fornix it feels as if rice grains lie embedded beneath the mucosa.

Schistosomal Nodules.—These are hard spheroidal bodies congested or pale in colour according to the degree of fibrosis underneath. They rarely bleed on contact. They are usually multiple but may be single.

Schistosomal Papillomata.—These are polypoid swellings with clubbed ends. They may be branched or have a single stem. They have the usual pink colour of the cervix but may be congested and haemorrhagic: they may then bleed on contact and their epithelium become ulcerated. Each papilloma has a central core of connective tissue continuous with the fibromuscular tissue of the cervix and containing many schistosome ova. These papillomata undergo enlargement during pregnancy, become more vascular and more friable, and bleed easily on touch, and their bases become broader and therefore more sessile. They are then easily mistaken for carcinoma.

Treatment

Schistosomal sandy spots, schistosomal diffuse infiltration, and schistosomal nodules respond well to tartar emetic, which is still the most effective treatment of

schistosomiasis. Schistosomal papillomata shrink under this treatment, but they usually need surgical excision or electric fulguration for their complete eradication.

Relation of Schistosomiasis of the Cervix to Cancer

A schistosomal lesion in the cervix may be mistaken for carcinoma. Confusion arises usually when infection or ulceration occurs. The changes that take place in schistosomal polypi during pregnancy may lead to an erroneous diagnosis of cancer.

It is difficult to say whether schistosomiasis predisposes to carcinoma of the genital tract or not. There is strong evidence that schistosomiasis of the bladder predisposes to carcinoma of that organ. Cancer of the bladder is common in Egypt, and its geographical distribution in the country corresponds to that of schistosomal infestation. It is also encountered at a relatively early age in patients who have had repeated schistosomal infestation of the bladder. It is claimed that toxic substances released from the miracidium irritate the epithelium (Ferguson, 1911). Dolbey and Mooro (1924) believe that cancer is induced by continuous irritation of the bladder by the alkaline urine, the bladder in these cases having been in a state of chronic cystitis for many years.

The presence of schistosome ova induces various changes in the epithelium which can be regarded as precancerous, such as basal-cell hyperactivity, leucoplakia, and even carcinoma *in situ*. No wonder then if one suspects schistosomiasis as a condition predisposing to cancer. However, carcinoma of the cervix on the top of schistosomiasis is not common. In the present series cancer in association with schistosomiasis of the cervix was encountered three times. This probably does not represent the true incidence, for it must be borne in mind that schistosomiasis of the cervix is often asymptomatic and many patients who have it do not present themselves for examination; if they develop cancer, however, they will certainly seek medical aid. Schistosomiasis has also been encountered in association with carcinoma of the cervix (Afifi, 1948; Charlewood *et al.*, 1949; Shafeek, 1957). It has also been observed in association with carcinoma of the vagina (Arean, 1956; Shafeek, 1957).

On the whole I feel that if schistosomiasis does predispose to cancer then it must be only rarely. Its rarity may be due to one or more of the following factors: (1) There may be a racial immunity against cancer of the cervix, for the disease is comparatively uncommon. It is noteworthy that circumcision of males is a routine ritual in Egypt. (2) Schistosomiasis is much less common in females than in males because the former are less liable to exposure to the infestation. Males get the disease when they come into contact with water in the irrigating canals. As a whole schistosomiasis of the genital tract is much less common than urinary schistosomiasis. (3) If the theory of irritation from alkaline urine is correct as an explanation for schistosomal cancer of the bladder, then the acid secretion of the vagina may have a protective influence against carcinoma of the cervix. (4) The bladder mucosa is continuously covered with urine and is not exposed to the atmosphere. The cervical mucosa, on the other hand, is exposed to it and has an easy drainage. This may have a protective action against any carcinogenic agent. The comparative rarity of carcinoma of the cervix with prolapse is well known.

Summary

Four interesting cases of schistosomiasis of the cervix are reported.

A study has been made of the clinical and pathological features of the disease based on a survey of cases of schistosomiasis of the female genital tract admitted to Kasr el Aini Hospital during 1950-60.

The possible relation of schistosomiasis of the cervix and carcinoma is mentioned.

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VENO-OCCLUSIVE DISEASE OF THE LIVER

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[WITH SPECIAL PLATE]

Veno-occlusive disease of the liver (V.O.D.) has a specific geographical distribution. The majority of cases are reported from Jamaica, where the disease was first recognized (Hill *et al.*, 1953; Jelliffe *et al.*, 1954a, 1954b; Bras *et al.*, 1954). In that area the disease occurs most commonly in children between 1½ and 3 years of age. It has three clinical and histological phases. The acute phase has an abrupt onset with hepatomegaly and ascites; the liver appears swollen and congested, and histological examination shows an intense centrilobular congestion with oedematous endophlebitis of smaller branches of the hepatic vein. There may be recovery from this phase or progression to the subacute phase, with persistent hepatomegaly which may also be associated with ascites; during this phase the central veins of the liver are blocked by a fibrous endophlebitis causing further centrilobular congestion with necrosis of liver cells and fibrous infiltration. This may progress to the chronic phase of centrilobular cirrhosis.

This disease is believed to be caused by ingestion of the senecio group of alkaloids. In Jamaica these occur in infusions of plants which are drunk as "bush teas." Experimentally, Berry and Bras (1957) have produced V.O.D. in a calf by feeding *crotalaria fulva*, an alkaloid of the senecio group, and Hill *et al.* (1958) have caused V.O.D. in rats by injections of monocrotaline, an extract of *crotalaria*, and by feeding of senecio. In cattle, seneciosis, which has a world-wide distribution, is a wasting disease with a V.O.D.-like affection as its essential feature.

Apart from the cases seen in Jamaica, there are reports of others from widely scattered areas. Wurm (1939) in Germany and Hashem (1939) in Egypt described