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 schistosoma 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.

REFERENCES

Afifi, M. A. (1948). *Bilharzial Cancer: Radiological Diagnosis and Treatment.* Lewis, London.
Arean, V. M. (1956). *Amer. J. Obstet. Gynec.*, **72**, 1038.
Charlewood, G. P., Shippel, S., and Renton, H. (1949). *J. Obstet. Gynaec. Brit. Emp.*, **56**, 367.
Dolbey, R. V., and Mooro, A. W. (1924). *Lancet*, **1**, 587.
Ferguson, A. R. (1911). *J. Path. Bact.*, **16**, 76.
Shafeek, M. A. (1957). *Gaz. Egypt. Soc. Gynaec. Obstet.*, **5**, 86.

VENO-OCCLUSIVE DISEASE OF THE LIVER

BY

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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

cases which were probably V.O.D. Selzer and Parker (1951) in South Africa reported senecio poisoning due to ingestion of bread made of contaminated wheat; this closely resembled V.O.D. Certain instances of Indian childhood cirrhosis have shown features of V.O.D. (Bras and Hill, 1956; Jelliffe *et al.*, 1957). Hill (1960) reports seeing a case from Israel. Three cases have previously been reported in children at this hospital (Stein, 1957).

From 1955 to 1960 we have seen 12 children suffering from V.O.D., and an analysis of these cases is presented in the Table.

Discussion

Of the 12 cases in this series, five were admitted in the acute phase and seven in the subacute phase; none showed frank cirrhosis. Figs. 1–3 on the Special Plate show the histology in a typical subacute case.

The three cases previously reported from this hospital (Stein, 1957) were all in babies under 18 months of age. This is in contrast to the age incidence in Jamaica, where the disease is rarely seen in children below that age. In the nine patients seen since 1957 this pattern has persisted; five of these were less than 18 months, the remaining four being between 18 and 30 months old. The sex incidence was equal—six males and six females.

Abdominal swelling was the presenting feature in all our cases. This had started from three days to four months before admission to hospital, with a maximum of one month in the acute cases. There was no family history of a similar illness in any instance. Administration of witch-doctors' or herbalists' medicines was admitted to in four cases; small amounts of the medicines were obtained in three of these, but on analysis none proved to contain senecio or related compounds. Foods were not analysed for toxic material.

Pronounced hepatomegaly was the most striking physical sign in all patients; eight had associated splenomegaly, three of these suffering from acute V.O.D. and five from subacute V.O.D. Ascites was present in nine cases and absent in three; the latter were all cases in the subacute phase with histories of illness varying between two and three months before admission. This corresponds with the experience in Jamaica, where ascites was more common and more severe in the acute phase. It would seem that with the progression of the disease a collateral circulation is established, allowing the ascites to subside.

The state of nutrition of the patients varied, but none appeared to be suffering from kwashiorkor, and in general these patients were better nourished than many of those admitted to our wards for other reasons; oedema of the legs was present in several patients and was almost certainly due to hepatic dysfunction, but there was no evidence of mucous-membrane changes or nutritional dermatosis. Serum protein levels were low in most of the cases, in keeping with liver damage. Thus malnutrition did not appear to be an aetiological factor. None of the patients had severe anaemia, only two having a haemoglobin level of less than 10 g. per 100 ml.

Only two children had clinical jaundice, one mild and one severe. Including these, the serum bilirubin level was raised above the normal of 1.2 mg. per 100 ml. in six patients, five of whom died. Thus there were no deaths among the cases with a normal serum bilirubin level. It is also of interest that the five deaths all occurred among children less than 15 months old. Death was precipitated by bronchopneumonia in two patients, by haematemesis in one, by haematemesis and associated hypoglycaemia in one, and by haematemesis and hepatic coma in one.

Only two of the seven survivors could be followed up for more than a year; both had been in the subacute phase of the disease and both recovered. In one case recovery was assessed on an increase in weight, regression of hepatosplenomegaly, and normal serum biochemistry. We were unable to obtain the parents' permission for a further liver biopsy in this case. In the other case a second liver biopsy ten months after the first revealed normal histology; this was in keeping with recovery as assessed clinically and biochemically.

In our experience V.O.D. has a high mortality rate. In Jamaica it has been established that this disease is almost certainly due to plant toxins and is therefore preventable. In South Africa, though we suspected that these toxins may be contained in witch-doctors' medicines, which are still quite commonly used among the native population, we have not been able to show

Analysis of 12 *Cases of Veno-occlusive Disease of the Liver in Children*

Case No.	Age in Months	Sex	Presenting Symptom	Ascites	Liver (cm. Below Costal Margin)	Spleen (cm. Below Costal Margin)	Jaundice	Serum Bilirubin (mg./100 ml.)	Serum Proteins (g./100 ml.)	Thymol Turbidity (Units)	V.O.D. Stage at Biopsy or Necropsy	Follow-up
1	14	F	Swollen legs and abdomen 1 month	++	3·0	—	—	2·2	3·5	5·5	Acute	Death from bronchopneumonia
2	5	F	Swollen abdomen 10 days	+	3·0	1·0	—	1·5	4·2	2·0	,,	,, ,,
3	12	F	Swollen abdomen 4 months	+	3·0	0·5	+	3·1	6·1	5·5	Subacute	Death from haematemesis
4	24	F	Swollen abdomen 2 months	—	3·0	1·5	—	0·5	5·1	3·5	,,	Survived; no follow-up
5	30	M	Swollen abdomen 3 months	—	2·0	1·0	—	1·0	4·0	4·0	,,	,, ,,
6	15	M	Swollen legs and abdomen 3 mths	—	3·0	2·0	—	1·8	4·5	2·5	,,	,, ,,
7	18	M	Swollen legs and abdomen 7 days	+	3·0	0·5	—	0·8	4·8	10·0	,,	Clinical recovery 2 years
8	11	M	Swollen abdomen 2 months	+	2·0	—	—	2·5	5·1	5·0	,,	Death from haematemesis and hypoglycaemia
9	3	F	Swollen abdomen 7 days	++	2·0	0·5	++	12·6	3·9	9·0	Acute	Death from haematemesis and hepatic coma
10	5	F	Swollen abdomen and legs 3 days	+	2·0	0·5	—	0·7	4·7	1·4	,,	Survived; no follow-up
11	8	M	Swollen abdomen 14 days	+	3·0	—	—	0·9	5·5	5·0	,,	,, ,,
12	22	M	Swollen abdomen and legs 7 days	+	3·0	—	—	0·8	4·9	3·5	Subacute	Complete recovery (biopsy)—10 mths

that this is the case. It remains possible that the toxic agent in our cases is contained in contaminated food. Further investigations of this source will be undertaken.

Summary

Veno-occlusive disease of the liver is discussed, particularly with reference to its aetiology and incidence. Twelve cases seen in African children are analysed. The age incidence of these cases was lower than in those reported from Jamaica, and it appeared in general that the younger the child the more likely he was to succumb to the illness. Another poor prognostic criterion appeared to be a raised serum bilirubin level; almost all patients with an abnormally high level died. A toxic aetiology in our cases has not been proved.

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REFERENCES

Berry, D. M., and Bras, G. (1957). *N. Amer. Vet.*, **38**, 323.
Bras, G., and Hill, K. R. (1956). *Lancet*, **2**, 161.
—— Jelliffe, D. B., and Stuart, K. L. (1954). *A.M.A. Arch. Path.*, **57**, 285.
Hashem, M. (1939). *J. Egypt. med. Ass.*, **22**, 319.
Hill, K. R. (1960). *Proc. roy. Soc. Med.*, **53**, 281.
—— Rhodes, K., Stafford, J. L., and Aub, R. (1953). *Brit. med. J.*, **1**, 117.
—— Stephenson, C. F., and Filshie, I. (1958). *Lancet*, **1**, 623.
Jelliffe, D. B., Bras, G., and Mukherjee, K. L. (1957). *Arch. Dis. Childh.*, **32**, 369.
—— —— and Stuart, K. L. (1954a). *Pediatrics*, **14**, 334.
—— —— —— (1954b). *Ann. trop. Med. Parasit.*, **48**, 386.
Selzer, G., and Parker, R. G. F. (1951). *Amer. J. Path.*, **27**, 885.
Stein, H. (1957). *Brit. med. J.*, **1**, 1496.
Wurm, H. (1939). *Klin. Wschr.*, **18**, 1527.

COMPARATIVE STUDY OF "VIRUGON" AND PENICILLIN IN MEASLES

BY

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Claims have been made in the pharmaceutical literature for the effective use in measles of the compound N′,N′-anhydrobis-(β-hydroxyethyl) biguanide hydrochloride (ABOB) marketed as "virugon." Farquhar (1960) reported the protective effect of virugon in hamsters inoculated intracerebrally with an adapted measles virus. He also reported a significant protective action when virugon was used prophylactically during a measles outbreak in a state school and, in another trial, noted no difference between five patients given virugon and five controls. The manufacturers state that a response is more likely if treatment is started early—for example, when Koplik's spots are present (personal communication).

This paper describes a comparative trial between penicillin V and virugon in 200 children with measles.

Penicillin (a syrup of penicillin V containing 125 mg. per 5 ml.) or virugon was given to alternate cases. Penicillin was given in 125-mg. doses four times daily for four days and virugon one tablet three times daily for seven days. No other treatment or antipyretics were given. At the first visit and on the fourth day thereafter a record was made of the temperature and pulse; also the presence or absence of tympanic injection, otitis media, and respiratory or other complications. In addition, at the first visit, the day of onset of the rash and an assessment of the severity of the illness were recorded. Revisits at other times were made as clinically necessary.

Of 200 patients, 10 were excluded from the trial—the majority because treatment was either not continuous or was not completed—96 patients received penicillin and 94 virugon. Sex and age are shown in Table I: there is a preponderance of children aged 0–2 in the penicillin group, but the difference is insignificant (P>0.05). There was no difference in severity between the groups (Table II) and no difference with regard to the day on which treatment was started (Table III).

TABLE I

	Sex		Age (Years)				
	Male	Female	0–	2–	4–	6–	8+
Penicillin	45	51	14	30	24	27	1
Virugon	42	52	5	32	26	25	6

TABLE II

	No. of Patients		
	Severe	Average	Mild
Penicillin	3	69	24
Virugon	3	62	29

TABLE III.—*Day on Which Treatment Began. (The Day on Which the Rash Appeared is Counted as Day 1)*

	Day				
	-1	0	1	2	3
Penicillin ..	0	7	60	28	1
Virugon ..	1	1	53	36	2

It was thought that a beneficial effect of virugon might be evidenced in two ways. Firstly, by a direct antiviral action in reducing the severity and/or duration of an uncomplicated illness. Secondly, by virtue of a reduction in severity the incidence of complications might be expected to be less. This postulate is made, as it has been demonstrated by the College of General Practitioners (1957) that there is a greater incidence of complications in the more severe cases. A clinical assessment of the severity of the illness on the fourth day proved impossible as the great majority of patients were much improved. A comparison of the fall in temperature between the first and fourth days showed no difference between the two groups. In the penicillin group the mean fall was 2.9° F. (S.D. 1.6) and in the virugon group it was 2.9° F. (S.D. 1.7). For the purposes of this paper complications were regarded as the

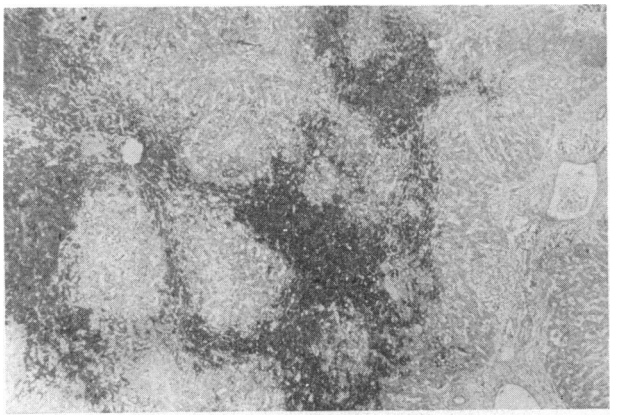

FIG. 1.—Section of liver showing intense centrilobular congestion. (H. and E. ×22.)

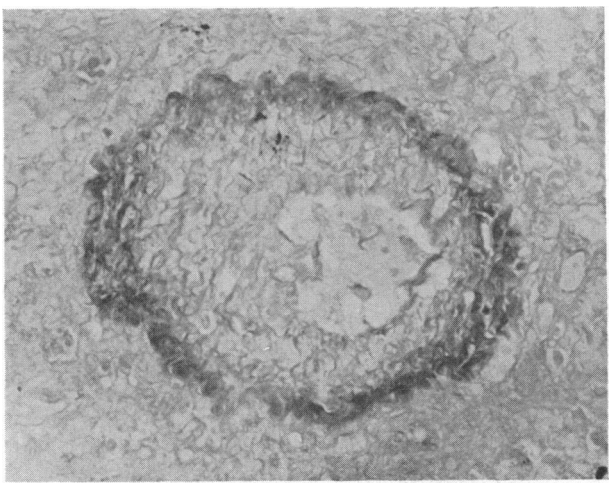

FIG. 2.—High-power view of a central vein showing fibrous endophlebitis. (Elastic van Gieson. ×200.)

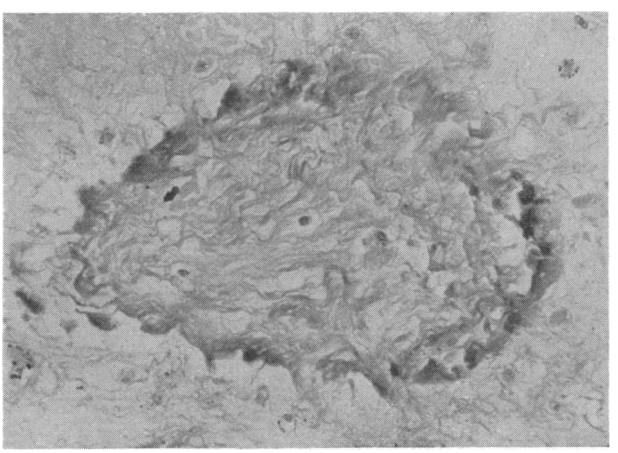

FIG. 3.—Central vein almost completely occluded. (Elastic van Gieson. ×288.)

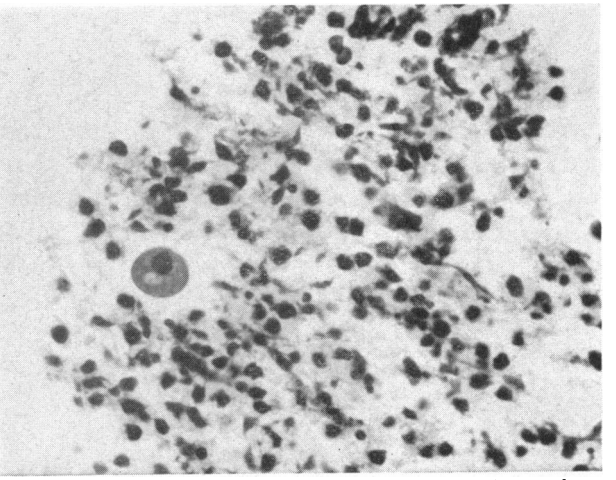

FIG. 1.—Section of necrotic tissue showing an amoeba, nuclear remains, lymphocytes, and occasional polymorphonuclear leucocytes. (H. and E. ×495.)

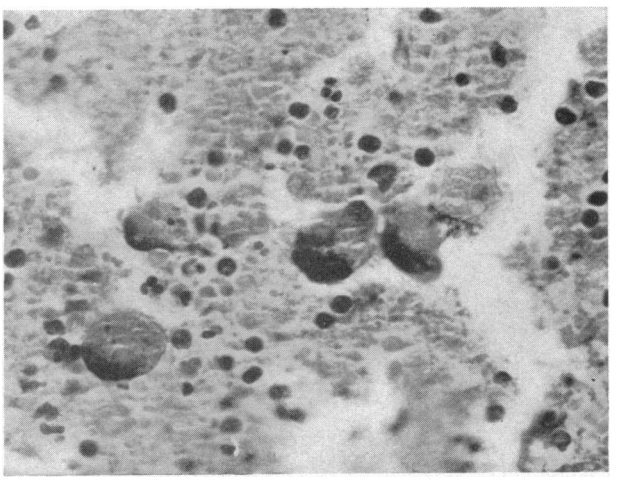

FIG. 2.—Section of necrotic liver tissue showing several vegetative forms of *Entamoeba histolytica*. A few contain phagocytosed red blood corpuscles. (P.A.S. ×495.)

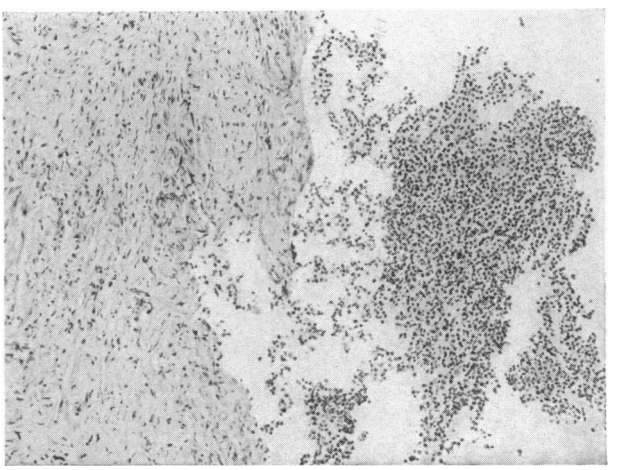

FIG. 3.—Low-power view of biopsy specimen showing fibrous tissue on left and necrotic tissue on right. (H. and E. ×75.)