micturition difficulty, and impotence in 2 each; and ileus in 1. Constipation and abdominal distension usually responded to vegetable laxatives taken at night. In only one case was constipation serious enough to lead to a true paralytic ileus, and this cleared completely after the drug was stopped. The infrequency of complaints of dryness of the mouth is notable in our series. This fact might be related to the local staple diet of steamed unripe banana ("matoke"), which has a soft porridge-like consistency. Matoke is likely to act as a demulcent in a dry mouth. The action of pempidine resembles that produced by mecamlamine on neuromuscular transmission, in that both drugs potentiate the effect of tubocurarine (Corne and Edge, 1958). Clinically, curare-like side-effects of muscular weakness, increased fatigability, and aching in the limbs were reported by 10 patients on continuous treatment. These side-effects do not appear to have occurred in other treatment series (Botha, 1959; Mathisen, 1959). In no case were the side-effects unduly severe. It is uncertain whether the additional fact of tropical heat has a part to play in the production of the curare-like effects recorded in this series. Blurred vision occurred in eight instances and, of the two who complained most bitterly, only one was literate and benefited from the use of glasses.

Effect of Chlorothiazides on the Fall in Blood-pressure due to Pempidine.—As with all other ganglion-blocking drugs (Smirk, 1959), the hypotensive action of pempidine was increased by the addition of 0.5 g. of chlorothiazide or 50 mg. of hydroflumethiazide, twice daily, together with 1.5 g. of potassium chloride. This regime was particularly effective in patients with heart failure.

Comparison of Mecamlamine and Pempidine.—If the effects of different ganglion-blocking drugs are to be compared accurately, it is necessary to make the comparison in the same patient at about the same time after the commencement of therapy. As we were unable to achieve such a comparison and as the side-effects of ganglion-blocking drugs are inclined to vary in the course of several months, an attempt to compare the effects of mecamlamine and pempidine was abandoned. The general impression gained was that there was no constant ratio between the effective dose of mecamlamine and pempidine in controlling blood-pressure. Little difference was noted in the incidence of side-effects in any one patient on each drug; the intensity and duration of side-effects were, however, distinctly less with pempidine.

Summary

Forty-three African patients with severe hypertension were treated with pempidine. Thirty-seven received treatment for from 4 weeks to 16 months—11 of them for 12 months or more. A complex regime proved successful under simple conditions.

Pempidine was shown to be an effective oral ganglion-blocking drug in most patients. In general, the advantages over mecamlamine were that continuous administration produced mild or moderate side-effects. Continuous therapy with pempidine did not lead to significant drug tolerance.

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PORTAL HYPERTENSION AND GROSS SPLENOMEGALY IN UGANDA

BY

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Gross splenomegaly is a common condition in Uganda (Trowell, 1950) as it is elsewhere in tropical countries (Fawdry, 1955; Chaudhuri, Saha, Basu, Mukherjee, and Rai Chaudhuri, 1956; Chaudhuri, 1957; Basu, 1958). The aetiology is often unknown. Liver disease, however, is common in Central African natives. A study of African patients with gross splenomegaly was therefore made, with the object of determining what relationship, if any, the splenomegaly bore to portal hypertension and liver disease. The results of this study are here reported.

Methods

All patients in whom the spleen was enlarged to the umbilicus and who were admitted to the medical unit at Mulago Hospital, Kampala, between September, 1955, and February, 1957, were studied. The method of investigation included a history, physical examination, full blood count, and various investigations to exclude splenomegaly due to leukaemia, active malaria, brucellosis, and schistosomiasis. Patients found to be suffering from these conditions were excluded from this study. As an index of portal-venous pressure the intra-splenic pressure was measured (Atkinson and Sherlock, 1954). Liver histology was studied by means of biopsy, and in 19 consecutive cases transplenic portal venography was carried out (Dreyer and Budtz-Olsen, 1952; Walker, Middlemiss, and Nanson, 1953).

Intrasplenic pressure was measured with a simple manometer; the pressure was taken routinely from three sites in the splenic pulp, except in patients with severe anaemia, in whom only one recording was taken. Clotting in the needle in the splenic pulp was troublesome in some of the earlier cases. The clotting-time

was therefore lengthened for the duration of the procedure by means of heparin and subsequently returned to normal with protamine (Sir James Learmonth, 1956, personal communication).

In the 11 patients who came to laparotomy, gastro-epiploic-venous pressure was measured directly and compared with intrasplenic pressure. In one case clotting had occurred at the intrasplenic measurement and a difference of 19 cm. was recorded between the intrasplenic pressure and the gastro-epiploic pressure. In two other cases the differences were 8 cm. and 6 cm. In the remaining eight cases the differences between the intrasplenic and gastro-epiploic-venous pressures were 4 cm. or less.

For control purposes, the intrasplenic pressure was measured in 11 medical in-patients, and the gastro-epiploic-venous pressure in seven surgical cases who came to laparotomy. In none of these cases was the spleen palpable.

Findings

The 47 cases studied comprised 36 males and 11 females, a similar sex distribution as for all medical admissions.

Intrasplenic pressure levels are shown in Fig 1. In 45 patients with splenomegaly, pressures varied from 3 to 50 cm. of saline. In 24 (53%) the pressure was over 25 cm. of saline, the average for the whole group being 28.2 cm. By contrast, in 18 control subjects without

FIG. 1.—Intrasplenic pressure levels in patients and control subjects.

splenomegaly a pressure of over 25 cm. was recorded in only one case. The average for this control group was 16.9 cm. of saline.

There appeared to be no correlation between the size of the spleen as estimated clinically and the height of the intrasplenic pressure, although in three cases in which the spleen became smaller subsequent measurement revealed a fall in intrasplenic pressure.

Liver biopsy was carried out in 41 cases. Severe fibrosis with destruction of architecture and nodular regeneration (cirrhosis) was present in five. In a further seven cases smaller degrees of portal fibrosis were present, moderate in four and slight in three. In the remaining 29 cases, fibrosis was not seen in the biopsy

sections. In these cases (Fig. 2) the liver sinusoids were infiltrated with lymphocytes, macrophages, and plasma cells. The portal tracts were in some cases, to a less extent, similarly affected. The degree of infiltration varied greatly and was slight in two cases. No significant changes were observed in the liver cells themselves.

(A good correlation was observed between the appearances of the liver at operation and the findings

FIG. 2.—Liver biopsy from patient with gross splenomegaly. Note lymphocytic infiltration of sinusoids and portal tracts. The intrasplenic pressure was 33 cm. of saline.

on biopsy. In two cases cirrhosis was noted at operation, and biopsy confirmed this finding. In one other case the surface of the liver was finally irregular and the consistency firm: biopsy revealed minimal portal scarring and moderate cellular infiltration. In the remaining cases in which no significant abnormality had been noted at operation (other than enlargement principally of the left lobe of the liver in one) biopsy revealed sinusoidal infiltration. In two of these latter cases the gastro-epiploic-venous pressures were 38 and 41 cm.)

In Fig. 3 the histological appearance of the liver and the level of intrasplenic pressure in each patient are shown. It is seen that high intrasplenic pressure was usually present in cases with hepatic fibrosis. The pressure was also raised in many cases in which there was no fibrosis but only infiltration of the sinusoids. The degrees of infiltration were not consistently associated with any particular levels of pressure, and in both cases in which infiltration was very slight the intrasplenic pressure was high.

An attempt was made to demonstrate an association between the height of the intrasplenic pressure and such

FIG. 3.—Histological appearance of the liver and intrasplenic pressure in 41 patients.

factors as the quality of the diet, a history of alcoholism, or the presence of anaemia, hypoproteinaemia, or ascites. However, with the doubtful exception of ascites, which may have been associated with the higher levels of intrasplenic pressure, these factors could not be related to the height of the intrasplenic pressure.

To exclude the possibility that extrahepatic portal obstruction was responsible for the raised intrasplenic pressures in these cases, transsplenic portal venography was carried out in 19 consecutive cases. No instance of extrahepatic obstruction was found. In one patient with advanced cirrhosis collateral circulation from the spleen to the stomach was demonstrated. In all cases the splenic vein was dilated and tortuous and, to a less extent, the portal vein was also dilated (Fig. 4). These appearances seemed to bear no relation to the height of the intrasplenic pressure, and in the three cases in which the pressure was below 25 cm. of saline the same changes were present. Intrahepatic branches of the portal vein were seen in 17 cases and were normal in 11. In six,

FIG. 4.—Venogram of patient with splenomegaly.

however, the primary branches of the portal vein were dilated, while the intermediate branches were narrow and poorly filled. The peripheral branches were normal. The reason for these changes was not apparent. The mean pressure in these six cases was not different from that in the remainder of the group and in five of the six fibrosis was not seen and the reason for the narrowing was not apparent.

Discussion

It may be emphasized that the changes in the livers of these patients with gross splenomegaly can be found in patients without gross splenomegaly or in necropsies on Africans with spleens of normal size. The degree of infiltration of the sinusoids in these cases was, however, much greater than was usually present in routine hospital necropsy specimens (J. N. P. Davies, 1955, personal communication). Similar changes have been reported (Fawdry, 1955) as occurring in gross splenomegaly in South Arabia.

Likewise, appearances on portal venography similar to those in the present series have been described as occurring in gross splenomegaly in Bengal (Basu and Das, 1956).

Attention may be drawn particularly to the finding of portal hypertension in the absence of hepatic cirrhosis or extrahepatic portal obstruction in the present study. The cause of this hypertension was not apparent. The measurements on control subjects show that the normal

portal-venous pressure is the same in the African as in the European. The lymphocytic cellular infiltration of some of the livers can also be excluded as the cause of the portal hypertension because in some cases where histological changes were marked the pressure was normal; in a few instances minimal histological change was associated with a raised pressure. Moreover, in three of the surgical "control" cases in which the gastro-epiploic-venous pressure was low infiltration was found in the liver biopsy specimen. It therefore seems that if these changes are concerned in the development of portal hypertension some other factor must also be present.

Measurements of intrasplenic pressure were made with the patient in the supine position. It has been suggested (Bull, 1948) that in this position the liver, if enlarged, may kink the hepatic vein and so cause a temporary obstruction throughout the portal system with a consequent rise in intrasplenic pressure. This explanation seems unlikely in the present cases, because of the 16 patients with an intrasplenic pressure above 25 cm. of saline and no fibrosis on liver biopsy the liver was clinically normal in size in 11, and only slight to moderate enlargement was present in the remaining five.

On venography and at laparotomy in these cases the splenic and portal veins were enlarged, and this suggests that the blood-flow through the spleen may be considerably increased in this idiopathic splenomegaly of Africans. Whether this might lead to an increase in pressure is uncertain. Possibly under conditions of increased blood-flow the infiltration in the liver sinusoids might act as an obstruction and lead to a rise in pressure. Walker (1959) has reported the occasional occurrence, in European subjects undergoing portocaval anastomosis for the relief of portal hypertension, of changes in the liver not unlike those of the present study, while Tisdale, Klatskin, and Glenn (1959) describe four cases in which portal hypertension and bleeding oesophageal varices occurred in the absence of both intrahepatic and extrahepatic obstruction of the portal vein. It was suggested by the latter authors that an increase in blood-flow may have led to the development of portal hypertension in these cases.

Summary

Forty-seven African patients with gross splenomegaly of unknown aetiology were studied. In 45 cases the intrasplenic pressure was measured; in 24 (53%) the pressure was over 25 cm. of saline. The average pressure for the group was 28.2 cm., compared with 16.9 cm. in 18 control cases without palpable spleens.

Liver biopsy carried out in 41 cases revealed varying degrees of hepatic fibrosis in 12. In 29 cases cellular infiltration of sinusoids and portal tracts was the main abnormality present. No evidence of extrahepatic portal obstruction was found in 19 consecutive cases on portal venography.

The common occurrence in this series of portal hypertension in the absence of hepatic fibrosis or of extrahepatic portal obstruction is discussed.

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NEW CASES OF G.P.I.

BY

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Is general paralysis of the insane (G.P.I.) becoming increasingly common to-day? This question has commanded our attention in recent months owing to the increasing number of cases we have seen. For some years now G.P.I. has been a rare disease. At one time it was relatively common, and wards full of these cases could be seen in most mental hospitals. To-day, of course, it is difficult to find cases of G.P.I. in mental hospitals. However, our experience in a busy psychiatric observation ward suggests that the disease is becoming more frequent. This ward is situated in a busy working-class north London district, drawing its patients from London, Middlesex, Essex, and Hertford. It has twelve beds and there are approximately 500 admissions per annum. Until two years ago only one, or perhaps two, cases of G.P.I. were admitted to this ward each year; these were invariably of long standing, had been treated, and were still showing psychiatric disturbance. However, during 1959 nine cases of G.P.I. were admitted to the observation ward. Steel (1960) described 14 cases of G.P.I. admitted to a 70-bed observation ward in the period April, 1957, to September, 1958. Our nine cases in a smaller unit and over a shorter period suggest that the frequency of G.P.I. is still increasing.

Most cases of G.P.I. present as psychiatric problems. In this paper the nine cases are described, particular attention being paid to the psychiatric picture.

Case 1

A man aged 65 was admitted from a general hospital, where he had been disturbed, aggressive, and confused after a laparotomy performed for abdominal pain. He laughed jovially at the slightest provocation, though he looked ill. His speech was rapid, words falling over each other, and punctuated by bursts of laughter. He frequently thumped the bed with his fists. He had florid, garish delusions of a grandiose nature, was grossly hallucinated both visually and aurally, and saw coloured men rushing at him and moving

his bed about. Three conjurers were in the ward trying to shoot him, and he roared with laughter as he described this. He was said to have had disseminated sclerosis over the past seven years which had affected his gait. At laparotomy no abnormality was found, and we believed that his pain was due to a tabetic crisis.

Physical Findings.—Slurred speech; partial Argyll Robertson pupils; left choroidoretinitis; brisk reflexes but diminished ankle-jerks and left extensor plantar response; loss of posterior-column sensation in the legs; positive Romberg's sign. Blood W.R. positive. C.S.F.: W.R. positive, cells 55 (mononuclear), protein 70 mg./100 ml., paretic Lange curve.

Psychiatric Picture.—A hypomanic confusional state with hallucinosis.

Case 2

A man aged 67 was admitted with a confusional state. He was bright, cheerful, euphoric, voluble, and visually hallucinated. There was a well-marked impairment of memory and he was disorientated for time, place, and person. He had a respiratory infection on admission and his hallucinations cleared up when his temperature became normal. He had Argyll Robertson pupils, increased tendon reflexes, and flexor plantar responses. Speech was a little slurred, and there was tremor of the tongue and fingers. Blood W.R. positive. C.S.F.: W.R. positive, cells 30 (mononuclear), protein 50 mg./100 ml., paretic Lange curve.

Psychiatric Picture.—A mild confusional state with memory impairment and disorientation. Hallucinations associated with respiratory infection; garrulous and over-talkative.

Case 3

This patient, a man aged 46, was admitted because of strange and violent behaviour at home, where he was no longer manageable. There was a gradual onset of deterioration in personality. He spent his money foolishly—for example, he bought many boxes of soap powder and half a dozen clocks—became violent-tempered and abusive; and would not tolerate disagreement by anyone. His memory became impaired during the past 18 months, especially for recent events, and latterly he made up fantastic stories. Often he was noisy, abusive, and violent, particularly when obstructed in any way, and threw food on the floor and smashed plates. He was restless and agitated. He had paranoid ideas about his wife, and thought that she had plenty of money which she kept from him. He gave a very poor account of himself and was often at a loss for words. A well-marked memory defect for recent events was apparent, and he tended to confabulate to cover up this deficiency. He was unable to describe or explain anything clearly. Mild disorientation was present. Though generally cheerful and co-operative he could be surly and suspicious at times. His main complaint was of impotence.

Physical Findings.—Slight slurring of speech; Argyll Robertson pupils; tremor of lips and tongue; reflexes normal. Blood and C.S.F., W.R. positive. Paretic Lange curve.

Psychiatric Picture.—A mild confusional state with impairment of memory and a Korsakoff syndrome. Aggressive, overactive, and hypomanic, with a paranoid background.

Case 4

A woman aged 69 was admitted because of confusion, inability to walk at times, and disturbance of memory. She became lost in her own house, was often incontinent, and had difficulty in speaking. She was said to have been suffering from an "anxiety state" for many years. In the past two years she had deteriorated gradually, and had been considered to be suffering from senile dementia. She had poor attention and comprehension. There was a marked impairment of memory, particularly for recent events. She was unable to perform the simplest calculations. She had a fatuous, silly smile and her mood was euphoric. She was quite disinterested in her constant incontinence.