establish the diagnosis is likely to arise where the condition is not suspected, and either the stools are not examined for amoebae or insufficient care is taken over the collection and handling of specimens. This was so in Case 1. The diagnosis in each of the cases was first suggested by the finding of large rounded mononuclear cells, containing ingested erythrocytes, lying in the tissues, and in two cases in the surface exudate. These cells had the morphology of vegetative *E. histolyticae*, and in spite of their large numbers could conceivably be confused with large macrophages showing erythrophagocytosis. Thus the discovery of these cells in a routine rectal biopsy does not furnish a conclusive diagnosis, but it at least indicates the need for a rigorous examination of the freshly passed stool, and, should this fail to reveal amoebae, a therapeutic trial with anti-amoebic drugs similar to that suggested by Paulley (1961) for cases of liver abscess of uncertain aetiology.

It is known that amoebic dysentery may masquerade as idiopathic ulcerative colitis; for example, in addition to the three cases now reported, Paulley mentioned that he had seen six, and Passarelli (1960) described *E. histolyticae* in five of 18 cases diagnosed as ulcerative colitis. Manson-Bahr (1943) reported the catastrophic results of surgery in the 1933 Chicago outbreak of amoebic dysentery, and Guthrie (1956) recorded the development of fatal amoebiasis cutis after surgery in an unsuspected case. Medical treatment with corticosteroids appears to be dangerous.

In an attempt to avoid further instances of delay in diagnosis the following recommendations are made:

(a) Rigorous bacteriological examination of all cases of ulcerative colitis, including microscopical examination of the freshly passed stool; examination of samples two to three hours old is of no value.

(b) An extensive search of biopsy material from cases of "ulcerative colitis" for morphologically identifiable vegetative *E. histolyticae* in the mucosa and submucosa, and particularly in the surface exudate. Recognition of amoebae is greatly facilitated by the use of the periodic-acid-Schiff method, by which they are coloured bright red.

(c) If only (b) above is positive, or if there remains doubt about the diagnosis, a therapeutic trial with amoebicidal drugs should be instituted. The toxic effects of emetine, for example, have been much exaggerated, and in practice the drug can be given in therapeutic doses without concern (Adams, 1960). The small risk of toxic effects is far outweighed by the possible benefits. If administration of these drugs resulted in preventing even one unnecessary colectomy per annum in a general hospital it would be worth while.

Summary

Three cases of amoebic dysentery initially thought to be examples of ulcerative colitis are described and discussed. In each case the diagnosis was indicated by histological examination of fixed biopsy material from the rectum or sigmoid colon. The importance of differentiating between amoebic and ulcerative colitis is stressed, and to facilitate this the following recommendations are made: (a) more rigorous protozoological examination of the stools in all cases of ulcerative colitis to exclude amoebic infection; (b) thorough search of the tissues and exudate of routine rectal and sigmoid biopsies for vegetative *E. histolyticae*; and (c) more frequent use of a therapeutic trial with amoebicidal drugs where indicated.

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BIOPSY OF THE RECTUM AS AN AID TO THE DIAGNOSIS OF AMYLOIDOSIS

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[WITH SPECIAL PLATE]

The examination of biopsy material is the most conclusive way of establishing a diagnosis of amyloidosis (Rukavina *et al.*, 1956). The primary form of amyloidosis so often affects the alimentary tract (Symmers, 1956; Thingstad, 1951) that biopsy of some part of the intestine might be expected to produce tissue containing the characteristic material, while in secondary amyloidosis the high incidence of intestinal involvement (in 55% of cases according to Dahlin, 1949) has been re-emphasized by Gafni and Sohar (1960), who used rectal biopsy to establish the diagnosis in 25 cases.

From the clinical material of a general hospital it has been apparent that, in patients suspected of having amyloidosis, useful information can be acquired by rectal biopsy. The purpose of this paper is to report the cases in which we have used this procedure to confirm the diagnosis of amyloid disease.

Method

A modified Truelove-Salt suction-biopsy instrument (Truelove *et al.*, 1955) was used to obtain biopsy specimens of the rectal mucosa. No special preparation of the bowel was required before instrumentation, but the presence of haemorrhagic disease was excluded by determining the platelet count and prothrombin time.

With the patient in the left lateral position a sigmoidoscope of the "cold-light" or "proximal-light" type was introduced from 5 to 15 cm. into the rectum. The biopsy instrument passed easily through the sigmoidoscope and the site of biopsy could be selected under direct vision. The procedure was painless and not associated with untoward sequelae.

The specimen was fixed in 10% formalin. Paraffin sections stained by haematoxylin and eosin, by methyl violet, and by congo red were examined. Microscopy always included examination by polarized light for congo-red birefringence (Pearse, 1960).

Amyloid material, when present, was found in the walls of small submucosal blood-vessels, both arterioles and venules (see Special Plate).

All the biopsies reported as containing amyloid material, when stained with methyl violet, have shown a metachromatic substance which has taken up congo red and has shown congo-red birefringence. At least ten sections were examined from each specimen before amyloid was excluded.

Results

Specimens were obtained by rectal biopsy from 24 patients, and in six of these amyloid material was demonstrated. The main clinical features of these cases are shown in Table I.

Rectal biopsy specimens from the remaining patients showed no demonstrable amyloid material. The essential details of these cases are summarized in Table II. Cases 7-19 were suffering from conditions liable,

on occasion, to be complicated by amyloidosis, though there was no collateral evidence to suggest that this had developed at the time of biopsy. However, Cases 20-24 presented some features which might have been due to amyloidosis, and for this reason are discussed later. Because of its special interest Case 20 is described briefly.

Case 20

A woman aged 40 had ulcerative colitis for four years when she noted recurrent pyrexial episodes during a period of ten months. She was found to have developed two large liver abscesses. There was a secondary amyloidosis with a blood urea value rising to 294 mg. per 100 ml., a markedly positive congo-red test (94%), and a very large liver. When the liver abscesses were drained surgically a liver biopsy showed marked parenchymal amyloid deposition. A right hemicolectomy was performed, and amyloid was also demonstrated histologically in the small submucosal vessels of the excised ulcerated bowel. At the time of rectal biopsy, nine months after operation, she was symptom-free and had gained weight. The hepatomegaly had resolved, her urine was free from protein, and the blood urea level had fallen to 60 mg. per 100 ml.

Discussion

Gafni and Sohar found evidence of amyloidosis on rectal biopsy in 26 out of 30 cases, which suggests that rectal involvement is common in patients with this disorder.

The value of tissue biopsy in a generalized disease depends on the technical ease and safety of the procedure, the frequency with which the tissue subjected to biopsy is affected, and also on the uniformity of

TABLE I.—Cases in which Rectal Biopsy Specimens Contained Amyloid Material

Case No.	Age (Years)	Clinical Diagnosis	Degree of Hepatomegaly	Blood Urea (mg./100 ml.)	Proteinuria (g./l. (Esbach))	Serum Albumin (g./100 ml.)	Other Information
1	48	Bronchiectasis; tuberculous pyonephrosis; nephrotic syndrome	Nil	27	5	1.2	Congo-red retention 47%
2	77	Syphilis with multiple gummata; nephrotic syndrome	Slight	45	5	1.6	" " 60%
3	57	Multiple myeloma with steatorrhoea	Nil	20	Nil	1.9	Subcutaneous nodules and jejunum showed amyloid
4	53	Rheumatoid arthritis; nephrotic syndrome	"	60-174	2	2.0	Liver biopsy showed amyloid
5	39	Bronchiectasis; ankylosing spondylitis; nephrotic syndrome	"	26	5-10	1.8	Congo-red retention 31%
6	60	Rheumatoid arthritis; nephrotic syndrome	"	40	+	3.5	" " 25%

TABLE II.—Cases in which Rectal Biopsy did not Show Amyloid Material

Case No.	Age (Years)	Clinical Diagnosis	Degree of Hepatomegaly	Blood Urea (mg./100 ml.)	Proteinuria (g./l. (Esbach))	Serum Albumin (g./100 ml.)	Congo-red Test (% Retention at 60 mins.)	Other Information
7	41	Bronchiectasis; rheumatoid arthritis	Nil	36	Nil	3.7	—	—
8	17	Ulcerative colitis	"	23	"	4.2	—	—
9	24	"	"	26	"	4.9	—	—
10	56	Ulcerative proctitis	"	42	"	4.7	—	—
11	49	Rheumatoid arthritis	"	24	"	3.7	—	—
12	56	Chronic tuberculous hip with discharging sinus	"	204	3	4.0	—	Renal and hepatic biopsies did not show amyloid
13	65	Nephrotic syndrome	"	27	2-12	1.5	46	Hepatic biopsy did not show amyloid
14	30	Bronchiectasis	"	36	Nil	5.5	18	—
15	29	Bilateral psoas abscesses; rheumatic heart disease; cirrhosis	10 cm. below costal margin	—	"	4.1	40	—
16	33	Nephrotic syndrome; psoriasis; rheumatic heart disease	Nil	24	0.8	1.9	—	Renal biopsy did not show amyloid
17	40	Bronchiectasis	"	24	0.0-5	4.5	—	—
18	48	Atypical myelomatosis	1 cm. below costal margin	92	0-trace	2.4	—	—
19	67	Polyarthritis; ? lupus psychosis	2 cm. below costal margin	36	Nil	3.6	—	—
20	41	Ulcerative colitis; liver abscesses	1 cm. below costal margin	60	"	4.3	—	Liver biopsy showed amyloid 9 months previously
21	65	Lichen cutaneous amyloid; polycythaemia vera	3 cm. below costal margin	36	"	5.7	—	Skin biopsy showed amyloid
22	26	Hodgkin's disease; nephrotic syndrome	Nil	24	2.0	2.5	—	—
23	47	Multiple myeloma; steatorrhoea	"	92	0.5	2.0	—	—
24	51	Rheumatoid arthritis; nephrotic syndrome	"	26-66	2-3	2.5	55	Gum biopsy did not show amyloid

distribution of lesions throughout that tissue. These criteria have been applied with varying degrees of success to biopsy of liver, kidney, skin, and gum. Biopsy of these tissues has, however, some practical limitations. Percutaneous needle biopsy of the liver is not entirely free from morbidity or mortality (Zamcheck and Sidman, 1953). It requires preparation of the patient and a moderate degree of proficiency from the operator, and it is not an out-patient procedure. Percutaneous renal biopsy has similar limitations, with possibly a greater risk of complications when performed by the inexpert. The skin is readily accessible, but probably the least satisfactory for diagnosis, since there is a low incidence of environment. Schilder (1909) found amyloid in sections of skin from seven out of 14 cases of advanced secondary amyloidosis. Cutaneous biopsy is most rewarding in the primary form of amyloidosis when involvement of the affected skin is self-evident. The gums are also accessible, though here biopsy is associated with some discomfort. Few authors have found the results of gum biopsy as rewarding as did Selikoff and Robitzeck (1947), who demonstrated amyloid in specimens of gum from 14 out of 18 cases with clinical evidence of secondary amyloidosis. Symmers (1956) commented that there were so few positive results that he thought gum biopsy was of little value.

Table III shows the assessments by various authors of the frequency of intestinal involvement in three forms of amyloidosis. The difference between the high incidence in Gafni and Sohar's cases and the lower

TABLE III.—Assessments of Frequency of Intestinal Involvement in Amyloidosis

Authors	No. of Cases in Series	Incidence of Intestinal Involvement (%)
Primary amyloidosis:		
Dahlin (1949)	8	100
Thingstad (1951)	54	61
Mathews (1954)	96	40
Symmers (1956)	145	70
Rukavina <i>et al.</i> (1956)	142	31
Secondary amyloidosis:		
Rosenblatt (1933)	125	2
Altnow <i>et al.</i> (1939)	50	22
Dahlin (1949)	30	55
Korelitz and Spindell (1956)	18	22
Gafni and Sohar (1960)	29	90
Amyloidosis secondary to myelomatosis:		
Bayrd and Bennett (1950)	3	33
Snapper <i>et al.</i> (1953)	8	87

incidence in the other authors' series may be due to the rapid post-mortem autolysis of intestinal tissue, which vitiates this type of study. Biopsy of living tissue may give a better estimate of this involvement than examination of necropsy material. The results presented here confirm the findings of Gafni and Sohar.

We have not found any "false negative" results of rectal biopsy in patients with proved generalized amyloidosis. Nevertheless it should be stressed that, though a positive result is diagnostic of amyloid disease, a negative one does not exclude it. There were six cases (Cases 20-24) in which clinical features suggested the possibility of amyloidosis but in which there was no evidence for this on rectal biopsy. In Case 20 the biopsy was taken nine months after drainage of liver abscesses and hemicolectomy. Rarely, regression of amyloidosis has been observed after elimination of the cause (Parkins and Bywaters, 1959), and it may have

occurred in this patient. The case of lichen amyloidosis (Case 21) had no clinical evidence to suggest systemic involvement, and localization of the process to the skin is characteristic of this condition (Ormsby and Montgomery, 1954). Case 22 was a 24-year-old female with Hodgkin's disease and a nephrotic syndrome. Case 24 was a female of 51 years who had suffered from rheumatoid arthritis for ten years and had developed a nephrotic syndrome; a gum biopsy and congo-red test were negative in this case. In neither case was renal biopsy performed, and the diagnosis remains in doubt. Case 23 had multiple myeloma and steatorrhoea, suggesting he might be suffering from amyloidosis of the small intestine.

Confusion may arise in the histological differentiation between amyloid and hyaline material when this is distributed in the walls of small blood-vessels. Montgomery and Muirhead (1954) demonstrated the affinity of hyaline for congo-red dye. However, the use of a control section in which amyloid is known to be present and examination for congo-red birefringence allow these types of infiltration to be distinguished. The affinity of hyaline for congo red is less than that of amyloid. Congo-red birefringence was not observed in hyaline Malpighian arterioles in sections of spleen; sections were taken from at least 15 cases. In addition, amyloid is often found in the walls of venules, while hyaline is restricted to arterioles.

Rectal biopsy has few practical limitations. There is negligible discomfort or danger, and the technique requires little special skill. The only complication is mild oozing of blood, which requires no treatment other than rest in bed.

Summary

Twenty-four cases were screened by rectal biopsy, and in six of these amyloid was found in the walls of small blood-vessels. There were no cases of proved amyloidosis with "negative" rectal biopsies, though four patients had some clinical features which may be attributable to this condition.

The demonstration of amyloid in biopsy material is the best available method of confirming a diagnosis of amyloidosis.

The frequency of intestinal involvement in amyloidosis is briefly discussed.

The ease of obtaining a rectal biopsy and the relative freedom from sequelae are emphasized, and the usefulness of rectal biopsy in the diagnosis of amyloidosis is confirmed.

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T. A. McALLISTER: DIAGNOSIS OF AMOEBIC COLITIS

FIG. 1.—Case 1. Vegetative *Entamoeba histolytica* containing ingested erythrocytes. These lie near surface of small ulcer. Note polymorphs in surrounding tissues. (H. and E. $\times 445$.)

FIG. 2.—Case 1. Vegetative *Entamoeba histolytica* in surface exudate. (P.A.S. $\times 1,005$.)

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FIG. 3.—Case 2. Vegetative *Entamoeba histolytica* in surface exudate. (H. and E. $\times 445$.)

Histological section of tissue obtained from Case 1, showing rectal submucosa with amyloid material in walls of small arterioles and venules stained by congo red (indicated by arrows). ($\times 120$.)

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HAEMODYNAMIC SHUNTS IN SCHISTOSOMAL COR PULMONALE

BY

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[WITH SPECIAL PLATE]

Schistosomiasis is an endemic disease in Egypt and is associated with a variety of visceral manifestations. The heavy invasion of the portal vein and tributaries by worms and ova leads to hepatosplenomegaly (Fig. A). In advanced cases the schistosome ova may embolize the lungs, lodging in the pulmonary arterioles and producing the picture of cor pulmonale (Zaky, 1952) with characteristic radiological findings (Special Plate, Figs. 1 and 2). This involvement of the portal and pulmonary circulations gives rise to important circulatory changes, and the haemodynamic shunts associated with these are the subject of this paper.

Material and Methods

Three patients with schistosomal cor pulmonale were studied by the following techniques.

1. Right heart catheterization was performed in the usual manner, but multiple samples of blood were withdrawn from the pre-pulmonary wedge position, midway to the hilum, right or left pulmonary artery, and the main pulmonary artery.

2. Dye-dilution technique, with injection of Evans (azovan) blue dye into the aorta and sampling from the pulmonary artery, to demonstrate an aorto-pulmonary shunt via the bronchial arteries. One cardiac catheter was advanced to the pre-wedge position in the pulmonary artery, while another was introduced into the brachial artery and advanced to the upper part of the descending aorta (Special Plate, Fig. 3). This position was chosen in order to avoid the mouths of the coronary arteries and short-circuiting of the dye through the coronary sinus. It also ensures that the bronchial arteries receive a good quantity of dye, since they arise a short way below the catheter tip. The capacity of each catheter was 2.8 ml. One operator injected 10 ml.

of Evans blue into the arterial catheter as rapidly as possible, but giving a signal at the 3-ml. level, at which moment the other operator began to withdraw from the venous catheter for five seconds. This was the first sample, and it averaged 4 ml. The syringe was changed and the second sample of 2 ml. withdrawn from the blood in the catheter. The first sample represented blood withdrawn from the pulmonary artery during the first $1\frac{1}{2}$ seconds, and the second sample that withdrawn between $1\frac{1}{2}$ and 4 seconds. The samples of blood were examined in a Beckman spectrophotometer for the presence of dye.

3. Aortic angiography with a balloon catheter to visualize the bronchial arteries and the pulmonary artery (Special Plate, Fig. 6). A No. 10 cardiac catheter had a rubber balloon fitted over the end hole, and two side holes were made proximal to this. The catheter was advanced via the brachial artery so that the tip lay in the descending aorta just below the lung hilum; 50 ml. of 76% "urografin" (sodium diatrizoate) was injected rapidly, causing the balloon to inflate and block aortic blood-flow, while the remainder of the contrast material escaped from the side holes. Radiographs were taken each second.

Results

Pulmonary Circulation

The presence of shunts between the bronchial arterial system and the pulmonary artery was suspected on the basis of two sets of observations (Zaky *et al.*, 1959). First, there was an absence of correlation between the size of the pulmonary artery and its luminal pressure. Gross dilatation of the pulmonary artery may be attended with a lower pressure than a smaller enlargement (Special Plate, Figs. 4 and 5). This was inferred to mean an increase in flow rather than in pressure to account for the discrepancy in size. Secondly, a progressive increase in oxygen saturation in the pulmonary artery was found as the catheter proceeded from the

FIG. A.—Patient with schistosomal hepatosplenomegaly.