PRIMARY INTESTINAL LYMPHOMA

A CHALLENGING PROBLEM IN ABDOMINAL PAIN

ZUHAIR R. AL-BAHRANI F.R.C.S.
Assistant Professor of Surgery

FARHAN BAKIR F.R.C.P.E.
Professor of Medicine

Department of Surgery and Medicine, Republic Hospital and Medical College, University of Baghdad, Iraq

Summary

PRIMARY INTESTINAL LYMPHOMA is not uncommon in Iraq. Forty-five cases were recognized in a nine-year period. The diagnosis is a puzzling challenge since lymphoma can simulate many medical or surgical conditions in the abdomen.

Pain is a constant complaint, loss of appetite and weight are very frequent symptoms. Fever, clubbing of the fingers and an abdominal mass are the commonly detected signs.

The erythrocyte sedimentation rate is often elevated. Careful radiological study may be helpful in diagnosis. The combination of such a clinical picture and supportive investigations should always raise the possibility of lymphoma.

Laparotomy is the most certain way of diagnosing the condition besides being of potential therapeutic value.

A RARE BUT not uncommon cause of persistent, unexplained abdominal pain in Iraq is primary intestinal lymphoma. This condition may simulate many diseases of the gastro-intestinal tract and is usually diagnosed late in its course. In the following report we have tried to give an idea about the incidence and the clinical features of the disease together with some of the helpful diagnostic criteria.

Material

Forty-five cases of primary lymphoma of the intestine were seen between 1962 and 1970, 25 of whom were diagnosed since 1968 as we became more aware and interested in the problem. The diagnosis was established in all by laparotomy and by subsequent histopathological examination. The disease was strictly localized to the intestinal tract with or without regional lymphadenopathy. Patients who had generalized lymphoma with intestinal involvement were not included. Their age ranged from $2\frac{1}{2}$ to 65 years. Twenty-one patients were below the age of 30 years, and only five were above the age of 50 years. The average age of the group was 29.9 years. Thirty of the patients were males and 15 were females (2 : 1). Thirty-six patients were Arabs and nine were Arians, four of them Kurds (Table I).

The majority of our patients came from the central part of Iraq, less from the north and few from the southern parts.

TABLE I

AGE AND SEX INCIDENCE IN 45 PATIENTS WITH PRIMARY INTESTINAL LYMPHOMA

Sex	*Age in years*							*Total*
	0–9	10–19	20–29	30–39	40–49	50–59	60–69	
M	2	4	5	11	4	2	2	30
F	3	1	6	2	2	1	–	15
Total	5	5	11	13	6	3	2	45

Presentation

The provisional clinical diagnoses after a careful history and thorough physical examination were as follows:

(*a*) Intestinal obstruction (14 patients—six of whom had an acute onset)
(*b*) Malabsorption (9)
(*c*) Abdominal neoplasm (8)
(*d*) Peptic ulcer (7)
(*e*) Peritonitis (3)
(*f*) Colitis (2)
(*g*) Ileocaecal tuberculosis (2)

All 45 patients had abdominal pain, which varied in its type, site, character, and its relationship to meals (Table II). Loss of weight was observed in 39 patients, and exceeded 10 Kg. in 21 of them. The appetite was poor in 26 cases. Vomiting was the next most frequent symptom and was seen in 31 patients. The bowel habit was variable. Fifteen patients were constipated, 13 had loose stool or diarrhoea which was quite severe in some. Eleven patients complained of acidity and heart-burn. In four cases the presenting complaint was abdominal swelling. Frank melaena was met with in four cases.

TABLE II

FEATURES OF ABDOMINAL PAIN IN 45 PATIENTS WITH PRIMARY INTESTINAL LYMPHOMA

Site		*Character*		*Relation to meal*		*Type*	
Generalized	11	Colicky	26	Unrelated	27	Intermittent	30
Umbilical	13						
Epigastric	12	Aching	15	Aggravated	14	Constant	15
Left side	5						
Right side	4	Hunger	4	Relief	4		

The duration of the illness was also variable: it was less than six months in 28 cases, and over 12 months in only six patients.

On physical examination all patients except three looked either acutely or chronically ill. Mild pallor was seen in some patients and it was severe and marked in two patients. Neither the liver nor the spleen was enlarged in any of the patients. Thirty-one patients were

febrile during the course of the illness and the temperature usually ranged from just over 37° C. to 38° C. Abdominal mass or masses were felt in 29 cases. Clubbing of the fingers was seen in 21 cases and in some it was very marked. The nails looked normal in 12 cases, and there were no statements about the nails in the remaining 12 cases. Signs of intestinal obstruction were present in 14 cases and signs of peritonitis in three (Table III).

The investigations were carried out on individual case bases, although the majority had a routine stool and urine examination. The haemoglobin estimation was less than 60% in five patients; it was 60–80% in 20 cases and in the rest it was above 80%. The E.S.R. was elevated in the majority. It was 20–40 mm./Hr. (Westergren) in 10 cases; it was above 40 mm./Hr. in 19 cases, and in only four patients the E.S.R. was 15–20 mm./Hr. The white cell count was usually normal. In the 9 patients

TABLE III

PROMINENT SYMPTOMS AND SIGNS IN 45 PATIENTS WITH PRIMARY INTESTINAL LYMPHOMA

Symptoms and signs	*No. of patients*
Abdominal pain	45
Weight loss	39
Vomiting	31
Fever	31
Abdominal mass	29
Poor appetite	26
Clubbing	21
'Intestinal obstruction'	14
Diarrhoea	13
Acidity	11
Melaena	4
'Peritonitis'	3

whose count was over 10,000/c.mm. with a relative increase of polymorphs, either had peritonitis or intestinal obstruction. The lymphocytes constituted over 30% of the count in only four patients, otherwise the differential count was within normal limits.

The chest radiogram was normal in all the 25 patients who were X-rayed.

The test for occult blood was done on 15 cases and it was positive in 10 of them, in addition to four patients with frank melaena.

Of the nine patients in the malabsorption group, beside the marked diarrhoea, the emaciation, the pallor and the abdominal distension, eight showed a malabsorption pattern on barium study. The D-xylose excretion test was abnormal. Low serum iron, calcium, and potassium, hypoproteinaemia and a flat glucose tolerance test were found whenever they were done.

Barium study

Barium follow-through was performed on 23 patients. In seven there were long irregular filling defects affecting a segment or multiple seg-

ments of the bowel, and in these malignancy was suspected (Fig. 1). In eight patients, the abnormal mucosal pattern of the bowel was diffuse simulating primary malabsorption (Fig. 2). 'Aneurysmal' dilatation or sacculation of the wall was clearly seen in three patients (Fig. 3), and in another two a localized annular stricture of the bowel was noticed. In three of these 23 patients barium meal revealed duodenal ulceration, while on laparotomy only two of them were found to have infiltration of the duodenal bulb by lymphoma (Fig. 4).

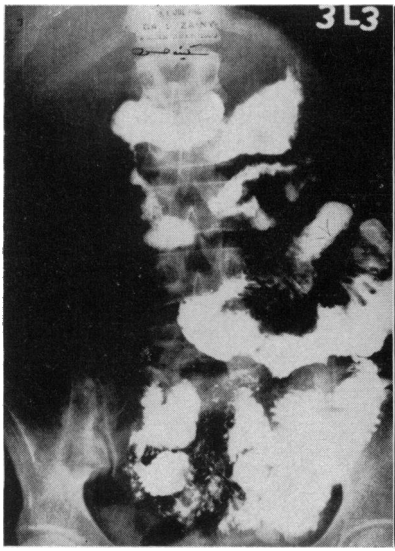

Fig. 1. Barium study of case 17 (S.H.), showing multiple filling defects and irregular mucosal pattern of upper jejunal loops.

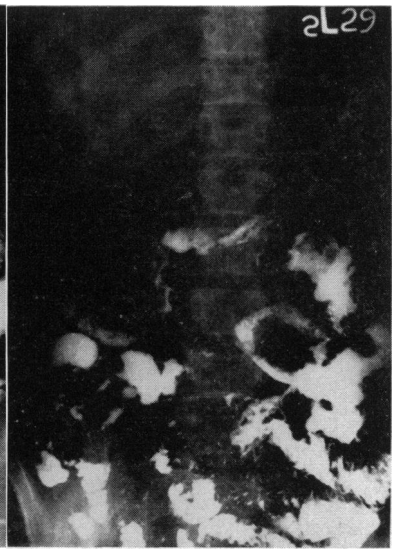

Fig. 2. Barium follow-through of case 22 (W.K.). The loss of normal mucosal contour, with segmentation and flocculation of barium, gives a picture of malabsorption.

Barium enema was performed in six patients because malignancy, tuberculosis, or colitis were suspected. In two patients positive findings were reported and these were cases of ileocaecal intussusception.

Operative findings and procedures

There were multicentric or skip lesions in 20 patients, it was unicentric in 13, and diffuse in the remaining 12. The most common site of lesion was the jejunum or near the duodenojejunal flexure. In 16 patients the jejunum alone was involved, the ileum alone in eight, the colon in two, and the duodenum in only one. There were multiple sites in 11 and the whole small bowel was affected in seven.

Mesenteric lymphadenopathy was a feature in most patients.

Fig. 3. Barium meal of case 45 (S.T.), illustrating 'aneurysmal' dilatation of upper jejunal loop, with loss of normal mucosal folds in the affected segment.

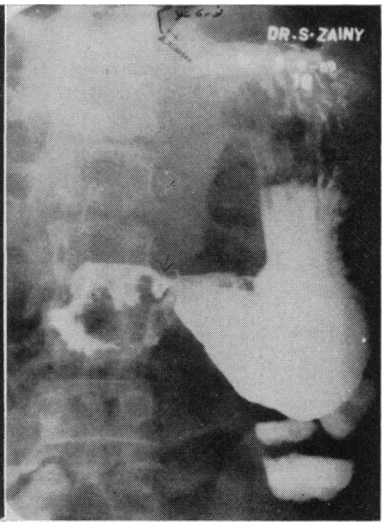

Fig. 4. Barium meal of case 41 (N.G.), showing gross deformity of duodenal cap suggestive of duodenal ulceration, which proved histologically to be caused by lymphomatous infiltration.

Extension of the tumour outside the intestinal wall was found in about half the patients. The liver and spleen were never involved.

Resection was possible in 23 patients, but in only 11 was this radical. In the remaining 22 patients the lesion was unresectable and in six of them a palliative by-pass procedure was performed.

Following surgery, cytotoxic drugs and/or deep X-ray therapy was given to most survivals (Table IV).

Histopathology

The gross appearance and the histological types are tabulated in Table V.

Results

Ten patients died in the immediate post-operative period. Five patients were not followed adequately after operation, while the remaining 30 patients were followed and seen at frequent intervals. The results in those 30 patients are summarised in Table VI.

TABLE IV

POST-OPERATIVE TREATMENT IN 35 FOLLOWED PATIENTS

Group of patients		*Cyclophosphamide*	*D.X.T**	*Cyclophosphamide and D.X.T.*	*None*
Resectable	18	8	4	2	4
Unresectable	17	11	2	4	-

*D.X.T. = Deep X-ray therapy

TABLE V

PATHOLOGICAL TYPES IN 45 PATIENTS WITH INTESTINAL LYMPHOMA

Gross appearance	*No. of patients*	*Microscopical appearance*	*No. of patients*
Infiltrative	20	Reticulum cell sarcoma ...	26
Nodular or fungating ...	9		
Excavating and ulcerative	8	Lymphosarcoma	15
Annular	3	Hodgkin's lymphoma ...	4
Mixed	5	Giant follicular lymphoma	0
Total	45	Total	45

ILLUSTRATIVE CASE REPORTS

Presenting as intestinal obstruction

S.H. (Case No. 17): 27 years old, female, complained of attacks of central colicky abdominal pain, vomiting, distension, and constipation for the last four months. She lost 20 Kg. of weight despite a good appetite. The significant findings were a temperature of 37.5° C. and a mobile mass felt in the umbilical area. Barium follow-through revealed an infiltrative lesion in the upper jejunum (Fig. 1). Provisional diagnosis = intestinal obstruction secondary to malignancy. On laparotomy multiple nodular lesions were seen in the upper jejunum causing partial obstruction (Fig. 5). Histopathology = Reticulum cell sarcoma.

Presenting as malabsorption

W.K. (Case No. 22): 22 years old, female, complained of epigastric pain after meals for the last six months. The appetite was poor, and she lost 12 Kg. of her weight. The bowel movement was frequent and the stool was loose. The temperature was 37.6° C., and clubbing was marked. The E.S.R. was 40 mm./Hr. Westergren, and the stool contained occult blood. Serum protein was 5.8 g. The D-xylose test was abnormal. Radiological study showed a malabsorption pattern (Fig. 2). Provisional diagnosis = malabsorption. Exploration = diffuse lymphomatous infiltration of the small bowel were seen (Fig. 6). Histopathology = reticulum cell sarcoma.

Presenting as duodenal ulcer

N.G. (Case No. 41): 32 years old, male, complained of epigastric pain of two years' duration, the pain was felt on eating and when hungry. (The hyperacidity and the pain eased when he vomited.) The appetite was good, yet he lost four Kg. of weight. However, he was well-built and well-nourished. There was epigastric tenderness. Mild clubbing was apparent. The E.S.R. was 55 mm./Hr. The first barium study revealed direct signs of duodenal ulceration. Because of the unsatisfactory response to treatment, a repeated barium study demonstrated the ulcer again, but in addition an abnormal mucosal pattern of the small bowel (Fig. 4). Provisional diagnosis = duodenal ulcer, lymphoma to be ruled out. At operation, duodenal ulceration was seen but the lymphomatous nature of it was only discovered when a pyloroplasty was attempted. Histopathology showed lymphosarcoma.

TABLE VI

FOLLOW-UP IN 30 PATIENTS WITH INTESTINAL LYMPHOMA

Period of follow-up	*Radical resection*		*Palliative resection*		*Unresectable*	
	Living	*Dead*	*Living*	*Dead*	*Living*	*Dead*
Less than ½ year			1	1		8
½–1 year		1		4	2	3
1–2 years	1	1		1		
2–4 years	4					
4–8 years	3					

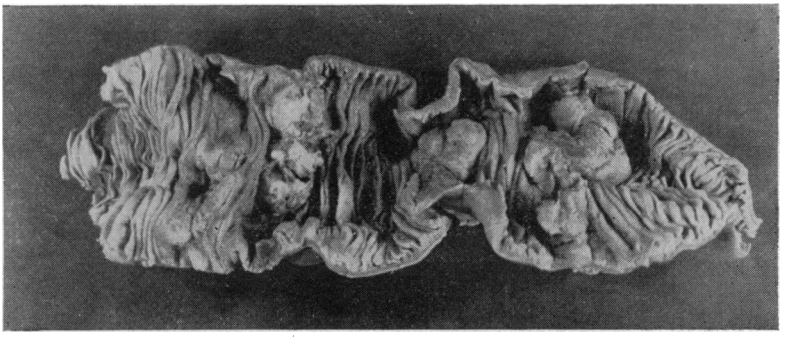

Fig. 5. Resected specimen of case 17, laid open. It shows multiple nodular lesions affecting the jejunum, causing partial intestinal obstruction.

Presenting as abdominal neoplasm

S.T. (Case No. 45): 36 years old, male, complained of epigastric pain, aggravated by food, of eight months' duration. The appetite was good, but he lost 10 Kg. of his weight. Temperature was 37.6° C., and clubbing was present. A mass was felt in the left hypochondrium. The E.S.R. was 107 mm./Hr. Barium study = infiltration and aneurysmal dilatation of an upper jejunal loop (Fig. 3). The clinical impression was malignancy. On laparotomy = sacculation of the upper jejunal loop and multiple nodular lesion in the lower jejunum (Figs. 7 and 8). Histopathology = reticulum cell sarcoma.

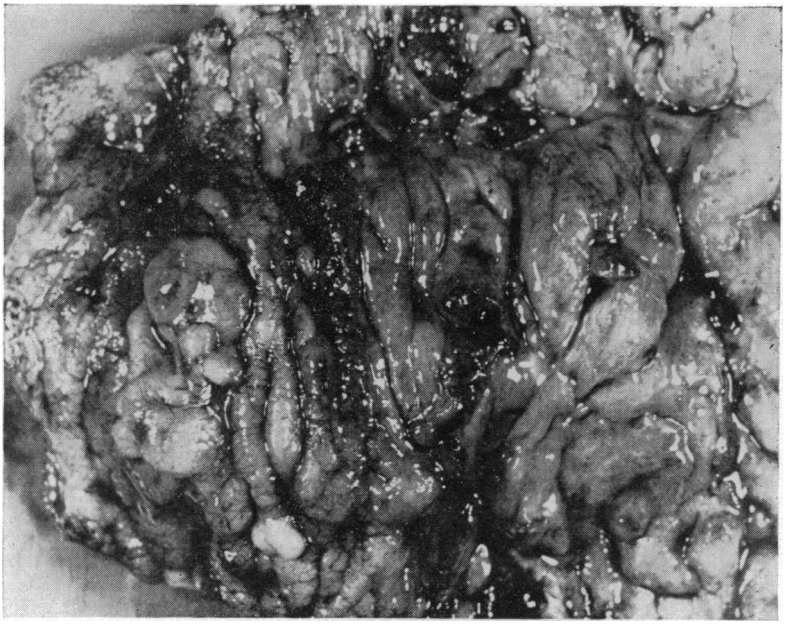

Fig. 6. Segment of the bowel resected from case 22. The open segment disclosing oedematous, swollen and finely nodular mucosa, but without ulceration. A typical appearance of the diffuse infiltrative form.

Discussion

The digestive tract may be involved in 5–32% of cases with generalized lymphoma[1], [2], [3]. Primary affection of the digestive tract by lymphoma has been reported to vary from 4 to 40%[4], [5], [6]. Many reports from Middle East suggest that the incidence of primary lymphoma is higher than from the Western World[7], [8], [9]. Our feeling is that it may be even higher in Iraq. At the same period of the study 495 cases of malignant neoplasms were seen in the same surgical unit as against 47 cases of small bowel malignancy, and of these 45 were cases of lymphoma. Unlike other series the small intestine was

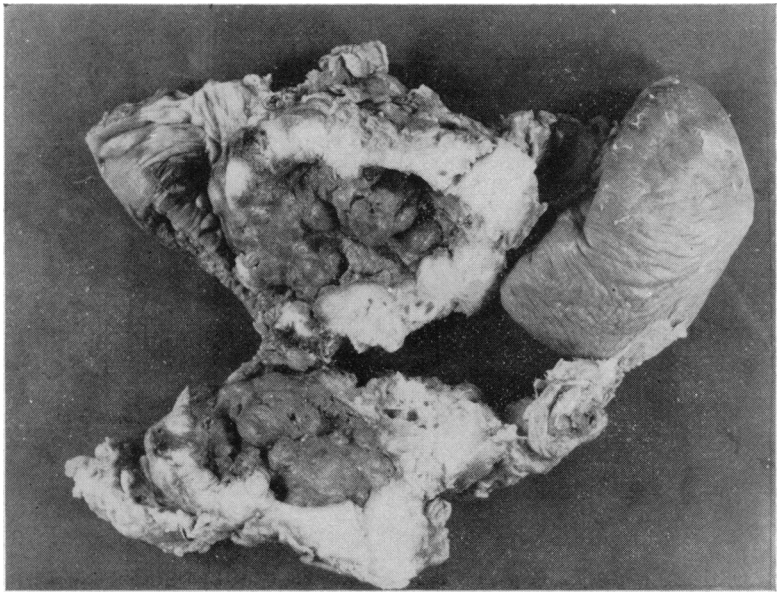

Fig. 7. Resected surgical specimen of case 45. It shows a dilated jejunal loop cut across, with thickening of the wall, taking the form of a saccular 'aneurysm'. The spleen was removed with part of the pancreas.

more commonly affected than the stomach[10], [2]. During the same period we have encountered only nine cases of gastric lymphoma. It is remarkable to see that lymphoma in Iraq affects a younger age group than cases reported from the West, and the lower age group is in agreement with other series reported from the area[7], [9]. The higher incidence among the younger age group should urge workers in the field to undertake wider epidemiological screening of the incidence of lymphoma. The exploration of a possible infectious agent in intestinal lymphoma of the Middle East has to be seriously considered.

The diagnosis of small bowel lymphoma has always been a challenging diagnostic problem in clinical practice[10], [11], [12]. This dilemma is more

true in a tropical or subtropical country like Iraq, where an abdominal complaint can be produced by a number of conditions which are much commoner than lymphoma.

A rewarding and useful diagnosis has to be made early and without too much unnecessary delay. When the disease has advanced to produce a palpable mass or peritonitis, it is usually beyond surgical help. The fact that about two-thirds of our cases were late arrivals or in a terminal state of the disease is an expression of the ignorance of the

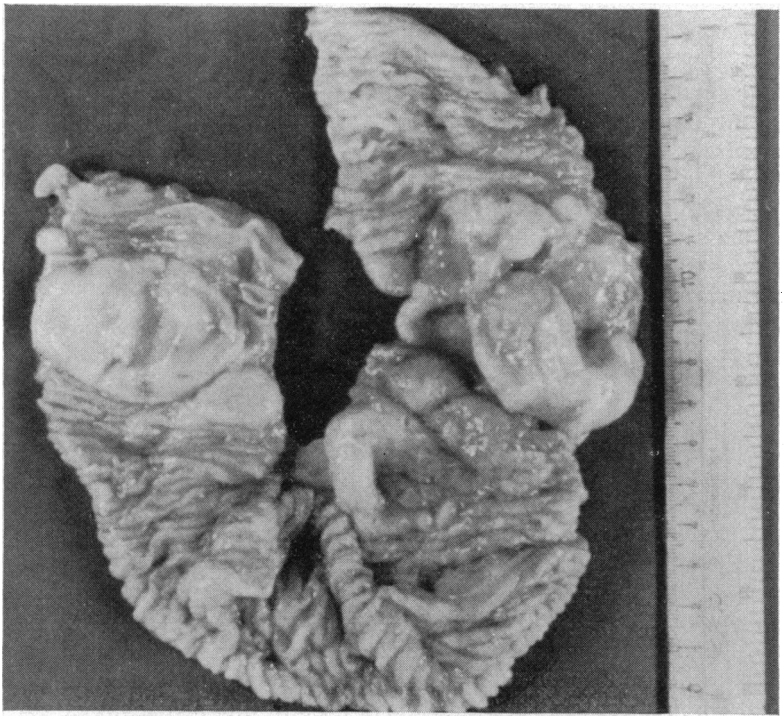

Fig. 8. The second resected specimen of case 45, which shows multiple nodular lesions in another segment of the jejunum.

condition, and in a good many of them a lengthy delay in sending them to our hospital took place because they were treated as different diseases.

Abdominal pain was an important feature, for it was present in every case. Furthermore it was the presenting symptom in about 80% of the cases. We found nothing specific or characteristic either in the type or the localization of the pain which could be of help in the diagnosis, but its presence, when added to other clinical parameters, such as loss of weight, lack of appetite, fever, clubbing, and an elevated E.S.R., should be enough to attract the attention to the possibility of lymphoma;

these at the same time should limit the differential diagnosis. Additional diagnostic investigations and the failure of the therapeutic trials should further narrow the diagnostic possibilities. We believe that every unexplained abdominal pain which is associated with the mentioned features should have the benefit of surgical exploration. The use of the intestinal biopsy capsule is limited, since intestinal lymphoma is of many types and one could miss a localized lesion easily, and even the multiple type of lesion may be missed. Besides, peroral biopsy is not without danger[13], [7]. Direct inspection by laparotomy is invaluable to see the involvement of lymph nodes, other organs, and to promote the correct therapeutic decision.

Intestinal lymphoma is one of the causes of malabsorption, but the high incidence among our cases (20%) is remarkable[14], [15]. The association of abdominal pain, the clubbing of the fingers, and the elevated E.S.R. in all the nine cases, the febrile course in seven, and the presence of masses in six, should be enough to direct attention to lymphoma as a possible cause. Pain is not a feature of malabsorption of other aetiology, clubbing is uncommonly seen in coeliac disease and fever is not a constant feature. The failure to respond to a gluten-free diet is helpful evidence against coeliac disease.

Careful analysis of the seven cases which simulated peptic ulcer should have helped to alter this erroneous diagnosis. Although the pain was typical in type and site to that of peptic ulceration, and all the patients were of the appropriate age group, and in spite of either a direct or indirect radiological evidence of ulcer, all the seven cases were found to have one or more unusual features of ulceration. Five were febrile during the course of the disease, clubbing was observed in five of them, and in three the appetite was poor. Three patients had an abnormal intestinal pattern in addition to the signs found in the duodenum, indicating the diffuse nature of the disease process. All these observations, added to a poor therapeutic response, should have raised some doubt about the diagnosis of peptic ulceration and have called for a more active diagnostic procedure, namely exploration.

Difficulty of diagnosis can even arise during operation, as intestinal lymphoma may simulate other conditions affecting the bowel, such as tuberculosis or Crohn's disease. Matting, calcification or caseation of the lymph nodes is against a diagnosis of lymphoma.

The prognosis appears to be affected by many factors, the most important in this respect are: early diagnosis, the site and distribution of the lesions, involvement of other organs, spread to regional lymph nodes, and complications of the tumour.

The response to cyclophosphamide or deep X-ray therapy was of short duration, and in no case proved of real value when surgery failed to eradicate the disease. Radical surgery alone, or followed by a course

of cyclophosphamide, gave the best results in our experience. It may be that the use of combination chemotherapy will be more effective and worth trying in future.

REFERENCES

1. SUGARBAKER, E. D., and CRAVER, L. F. (1940) *J.A.M.A.* **115**, 17–23.
2. ROSENBERG, S. A., DIAMOND, H. D., JASLOWITZ, B., and CRAVER, L. F. (1961) *Medicine*, **40**, 31–84.
3. WELBORN, J. K., REBUCK, J. W., and PONKA, J. L. (1967) *Arch. Surg.* **94**, 717–723.
4. GALL, E. A., and MALLORY, T. B. (1941) *Ann. Intern. Med.* **14**, 2073–2090.
5. DARGEON, H. W. (1953) "Lymphosarcoma in childhood", *Advances in Pediatrics*, **6**, 13.
6. BROOKES, V. S. (1968) *Proc. Roy. Soc. Med.* **61**, 216–217.
7. EIDELMAN, S., PARKINS, R. A., and RUBIN, C. E. (1966) *Medicine (Balt.)* **45**, 111–137.
8. GEDEON, E. M. (1970) *Leb. Med. J.* **23**, 1–10.
9. NASR, K., HAGHIGHI, P., BAKHSHANDEH, K., and HAGHSHENA, M. (1970) *Gut*, **11**, 673–678.
10. ALLEN, A. W., DONALDSON, G., SNIFFEN, R. C., and GOODALE, F. (1954) *Ann. Surg.* **140**, 428–438.
11. PAGTALUNAN, R. J. G., MAYO, C. W., and DOCKERTY, M. D. (1964) *Am. J. Surg.* **108**, 13–18.
12. SCHMUTZER, K. J., HOLLERAN, W. M., and REGAN, J. F. (1964) *Am. J. Surg.* **108**, 270–276.
13. CUPPS, R. E., HODGSON, J. R., DOCKERTY, M. B., and ADSON, M. A. (1969) *Radiology*, **92**, 1355–1362.
14. FLICK, A. L. QUINTON, W. E., and RUBIN, C. E. (1961) *Gastroenterology*, **40**, 120–126.
15. FAULKNER, J. W., and DOCKERTY, M. G. (1952) *Surg. Gynec. Obstet.* **95**, 76–84.
16. KENT, T. H. (1964) *Arch. Path.* **78**, 97–103.

Council Meeting

AT AN EXTRAORDINARY MEETING of the Council on 7th July 1971, with Sir Thomas Holmes Sellors, President, in the Chair, Professor Jonathan Rhoads, M.D., was admitted to the Honorary Fellowship.

Professor Ralph Cocker and Dr. Frank Stansfield were admitted to the Fellowship by election, and Mr. Denys Wainwright was admitted to the Fellowship *ad eundem*.

Diplomas of Fellowship were granted to the candidates named in the Report of the Court of Examiners.

A Diploma of Fellowship in the Faculty of Anaesthetists was granted to Hossam Nayel of Glamorgan.

One hundred and sixty Diplomates were presented, in order of Medical and Dental Schools, as follows: Fellows; Fellows in Dental Surgery; Fellows in the Faculty of Anaesthetists; Members; Licentiates in Dental Surgery.

Professor Jonathan E. Rhoads, M.D., of the University of Pennsylvania, delivered an address to the new diplomates (to be published).