impaired, and therefore local intoxication and malnutrition of the parenchymal elements must follow the initial stage of disturbed capillary permeability. This has been pointed out by Eppinger *et al.* (1935), as well as the fact that excessive amounts of serum proteins in the perisinusoidal spaces may well lead to the invasion of the parenchymal cells by serum proteins and by serum enzymes, resulting in damage to the cell (Böck and Popper, 1937).

The final picture of serous hepatitis is diffuse hepatic fibrosis. This has been arrived at by a slowly progressive fibrosis, intralobular and also perilobular in distribution, which occurs in the coagulum deposited in these positions. A theory has been postulated which attempts to explain the pathogenesis of this fibrosis.

Serous hepatitis, then, may well be one of the causes of polylobular cirrhosis, which Dible (1951) refers to as "cryptogenic."

Summary

A liver disease occurring in Jamaican children has been described; because of its clinico-pathological aspects it has been named "serous hepatitis." To date the only aetiological factor which has been ascertained is a low dietary protein intake. It is suggested that toxic factors may also play a part.

Clinically, the condition occurs in children, usually between the ages of 1 and 3 years, who have an enlarged firm liver and ascites; ultimately the appearance may be one of classical hepatic cirrhosis.

Histologically, the disease is a progressive one, passing from an initial exudation or oedema to the deposition of an eosinophilic coagulum which is finally invaded by fibroblasts.

The condition is similar to that described by Roessle (1930) as "serous hepatitis."

A theory of the pathogenesis of liver fibrosis has been postulated.

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TREATMENT AND PROGNOSIS OF ACUTE PERFORATED PEPTIC ULCER

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During the last decade there has been a striking fall in the fatality of acute perforated peptic ulcer. Whereas before 1942 the operation mortality was commonly 20%, the figure to-day is not more than a quarter of that level. This fall can mainly be attributed to improvements in anaesthesia with the introduction of muscle relaxants and to the use of antibiotics. Deaths from peritonitis in the first week have almost ceased to occur, and fatal cases are now mainly due to concomitant bleeding, intestinal obstruction, and associated diseases. This was demonstrated in the series reported by Avery Jones, Parsons, and White (1950). With the reduction in fatality, interest has been aroused in new methods of management.

Three methods are currently recommended—medical management with gastric aspiration, simple surgical closure, and immediate partial gastrectomy. The choice, in the individual case, must depend on the facilities available, but it will be influenced by knowledge of the immediate and late prognosis in similar cases treated by each method, and it will not necessarily be the same for all patients. It is difficult, on the existing evidence, to assess the relative merits of the three methods, partly because the fatality associated with each method has been rapidly decreasing, and partly because insufficient attention has been paid to the end-results, after the patients have left hospital.

The series reported by Avery Jones, Parsons, and White included 490 patients treated at the Central Middlesex Hospital during 1938–48, the great majority of them by simple surgical closure of the perforation. Since 1948 patients at the hospital have, in the main, continued to be treated by the same method, and the results have been analysed for a further period of three years to see, first, whether the fatality has continued

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to fall; secondly, whether a figure can be obtained for the fatality from surgical closure for comparison with the results obtained by other methods; and, thirdly, whether indications can be defined for the choice of patient to be treated medically with gastric aspiration or by immediate partial gastrectomy.

Immediate Prognosis

Table I shows the number of patients, operated and unoperated, with the corresponding number of deaths each year from 1938 to 1951. Patients diagnosed as having "leaking ulcers" are not included. The table shows that there has been no recognizable change in fatality since the beginning of 1947, when the standard

interest that the sole patient who recovered without operation prior to 1947 was shown radiographically to have a gastric ulcer after recovery from the perforation and died five years later from a slowly growing carcinoma originating in the same part of the stomach.

Surgical Closure of the Perforation

The crude fatality rate is of limited value for comparative purposes, since fatality also depends on a number of factors other than treatment, and these are not always constant. Factors usually considered to influence the fatality of perforated ulcers are the sex and age of the patient, the site of the ulcer, and the duration of the delay between onset and institution of treatment. From the experience of the results in the whole series of surgically treated cases,

TABLE I.—Prevalence and Fatality of Perforated Peptic Ulcers, 1938–51; Operated and Unoperated Cases

Year:	1938	1939	1940	1941	1942	1943	1944	1945	1946	1938–46	1947	1948	1949	1950	1951	1947–51	1938–51
Patients operated on	39	35	32	38	33	44	41	41	46	349	52	54	64	67	83	320	669
No. of deaths	12	8	7	7	11	3	4	5	3	60	3	1	0	3	3	10	70
Patients not operated on*	0	1	0	2	2	3	7	4	7	26	6	3	5	2	4	20	46
No. of deaths	0	1	0	2	2	3	6	4	7	25	5	2	5	2	3	17	42
Total perforations	39	36	32	40	35	47	48	45	53	375	58	57	69	69	87	340	715
No. of deaths	12	9	7	9	13	6	10	9	10	85	8	3	5	5	6	27	112

* Necropsy examinations were performed more frequently in the later years, and it is possible that some fatal perforations were missed in the period 1938–42.

treatment described by Avery Jones, Parsons, and White was adopted. In the five years 1947–51 the total fatality in 340 cases, including those undiagnosed till after death, was 7.9%. The operative mortality in 320 cases was 3.1%. Nineteen patients were treated by immediate partial gastrectomy without a death and 301 were treated by surgical closure of the perforation with 10 deaths, giving a mortality of 3.3%.

Unoperated Cases

Forty-six patients were not operated on. Medical treatment did not include the use of gastric aspiration until after 1946; since then it has been used routinely in cases diagnosed in life. The reasons for which operation was withheld and the results of treatment are given in Table II.

TABLE II

	1938–46		1947–51	
	Cases	Deaths	Cases	Deaths
Perforation undiagnosed ..	12	12	5	5
Patient too ill	13	12	9	9
Medical treatment preferred ..	1	1	5	3
Operation refused	—	—	1	0

One diagnostic error was failure to recognize perforation in patients who had recently had a severe haematemesis or melaena; the diagnosis in this group was sometimes particularly difficult because of the presence of peripheral circulatory failure and the lack of abdominal tenderness and rigidity. The double complication was unrecognized in six instances, all during the period 1938–46. Other patients were thought to have coronary thrombosis, mesenteric thrombosis, or carcinomatosis; others came into hospital unconscious and no diagnosis was made.

The majority of the patients in whom perforation was diagnosed and who were not operated on had peripheral circulatory failure and could not be resuscitated sufficiently for operation; they cannot be used for assessing the results of medical treatment. It is, however, of

it can be shown that differences in the fatality rate in men and women can be adequately explained by the greater proportion of women among patients with gastric perforations and among those in whom operation is delayed more than 12 hours. On the other hand, the age of the patient, the site of the ulcer, and the duration of delay all affected the fatality independently of one another. The results are shown in Table III. The expected numbers of deaths have

TABLE III.—Fatality of Perforated Gastric and Duodenal Ulcers Treated Surgically, 1938–51. Subdivided by Sex and Age of Patient, Site of Ulcer, and Duration of Delay Before Treatment*

Factor Affecting Fatality	No. of Cases	No. of Deaths		Factor Affecting Fatality	No. of Cases	No. of Deaths	
		Obs.	Exp.			Obs.	Exp.
Sex:				Site:			
Male ..	598	62	62.5	Stomach ..	122	27	16.4
Female ..	53	7	6.5	Duodenum ..	529	42	52.6
Age:				Duration of delay:			
Under 35 ..	146	7	13.1	Less than 6 hr.	370	25	33.6
35–44 ..	155	5	13.6	6–11 hr. ..	197	15	23.1
45–54 ..	161	19	15.6	12–17 ..	43	11	7.1
55–64 ..	118	24	16.4	18 hr. and over	41	18	5.2
65 and over ..	71	14	10.3				

* Eight cases with one death have been omitted because the case records were incomplete, and 10 cases of perforated jejunal ulcer with no deaths have been excluded as being too few for separate analysis.

been calculated by allowing for the effects of all the other factors under consideration. For example, to obtain the expected numbers of deaths in men and in women, the numbers of men and of women with perforations in each age, site, and duration of delay subgroup were multiplied by the fatality rate for persons in that subgroup and the resulting products for each subgroup were added.

The excess mortality from perforated gastric ulcers is striking; it occurred in each age group, but to a significant extent only when the duration of delay was less than six hours (Table IV). The reason for the excess mortality

TABLE IV.—Duration of Delay

Hours:	Less than 6	6–11	12–17	18 +
Duodenal perforations:				
Observed deaths ..	11	9	7	15
Expected	20.5	10.9	7.0	14.2
Gastric perforations:				
Observed deaths ..	14	6	4	3
Expected	4.5	4.1	4.0	3.8

from gastric ulcers in the group of patients who reach hospital without much delay may perhaps be that very large perforations occur more readily in gastric ulcers and that these result in immediate massive soiling of the peritoneum and also bring the patient rapidly to hospital with urgent symptoms.

Whether the same factors continue to influence the fatality rate now that it has been greatly reduced cannot yet be determined; the presumption must be that they do. The results for the period 1947-51 are therefore shown in Table V, subdivided by age of the patient, site of the ulcer,

TABLE V.—*Fatality of Perforated Gastric and Duodenal Ulcers Treated by Surgical Closure of the Perforation, 1947-51; Subdivided by Age of the Patient, Site of Ulcer, and Duration of Delay Before Treatment**

Age of Patient	Duration of Delay in Hours					All Durations
	Less than 6	6-11	12-17	18+	Not Known	
<i>Duodenal Ulcers</i>						
Under 35 ..	45	20	1	3 (1)†	0	69 (1)
35-44 ..	38 (1)	22	3	2	3	68 (1)
45-54 ..	39 (1)	23	3	1	0	66 (1)
55-64 ..	12	12	2 (1)	1	0	27 (1)
65 and over ..	13 (1)	7	5	2 (1)	1 (1)	28 (3)
All ages ..	147 (3)	84	14 (1)	9 (2)	4 (1)	258 (7)
<i>Gastric Ulcers</i>						
Under 35 ..	3	2	1	0	0	6
35-44 ..	5	1	0	0	0	6
45-54 ..	3	3 (1)	1	1	0	8 (1)
55-64 ..	3	6	2 (1)	2	0	13 (1)
65 and over ..	2 (1)	2	2	0	1	7 (1)
All ages ..	16 (1)	14 (1)	6 (1)	3	1	40 (3)

* In the same period three patients with perforated jejunal ulcers were also treated by surgical closure of the perforation; all survived.
† The numbers of fatal cases are shown in parentheses.

TABLE VI

Cause of Death	No.	Sex	Age	
Death during induction of anaesthetic	1	M	68	D.U.
Post-operative shock (i.e., death within 48 hours of operation and including early death due to peritonitis) ..	2	M	64	D.U.
		M	69	D.U.
Chest infections	2	M	59	G.U.
		M	70	G.U.
Haemorrhage from the ulcer (3rd to 22nd day)	3	M	47	D.U.
		M	47	G.U.
		M	69	D.U.
Intestinal obstruction (13th day) ..	1	M	43	D.U.
Pulmonary embolus (22nd day; following further laparotomy) ..	1	M	24	D.U.

and duration of delay, so that any part played by these factors can be allowed for in assessing the significance of the overall fatality rate. The causes of death in the ten fatal cases are given in Table VI. More radical treatment of the ulcer at the time of perforation might perhaps have reduced the fatality by eliminating the possibility of subsequent haemorrhage.

Partial Gastrectomy

Since the beginning of 1948 selected patients have been treated by partial gastrectomy. Up to the end of 1951, 19 patients had been so treated without a fatality; in the first six months of 1952 the number has been increased to 30. The total is too small for detailed comparison of the results with those obtained by surgical closure, but it would at least appear that the immediate prognosis is good enough to justify continuing with the treatment. The patients were to some extent selected to exclude bad risks—for example, no patient was aged more than 65—but, on the other hand, five patients were specifically treated by this method because of the dangerous association of haemorrhage with the perforation.

The operations have been performed by a number of surgeons, and the indications for the choice of the method of treatment have been varied; they are discussed in detail later.

Association of Haemorrhage and Perforation

Thirty-four patients in the series presented with a perforated ulcer within a fortnight of having had a haematemesis or a melaena; most commonly the haemorrhage had occurred within the preceding 24 hours. In six instances the perforation was unrecognized till after death. The results of treatment in the 28 diagnosed cases are shown in Table VII.

TABLE VII

	1938-46		1947-51	
	Cases	Deaths	Cases	Deaths
Medical treatment ..	—	—	2	2
Surgical closure ..	13	6	8*	1
Partial gastrectomy ..	—	—	5	0

* Including one case of perforated jejunal ulcer.

Until 1947 the association of the two conditions gave rise to a very high fatality rate. Since then the results would appear to have been better, irrespective of the type of surgical treatment employed. The numbers are, however, too small to justify a confident conclusion. The two patients treated medically were aged 71 and 86, and medical treatment was considered preferable because of their age; both died. As a result of this experience, surgery is now preferred if it is at all feasible, and two further cases occurring in men aged 71 have been treated successfully by surgical closure of the perforation. The oldest patient treated by partial gastrectomy was 63.

In 40 patients haemorrhage occurred after treatment of the perforation had been instituted. Five of these were patients included above who had also bled with or shortly before their perforation and in whom the perforation had been treated by surgical closure; four died. In another fatal case the haemorrhage appeared after a perforation which was not operated on. In the remaining 34 patients haemorrhage appeared after surgical closure of the perforation; the results of treatment are given in Table VIII.

TABLE VIII

Treatment of the Haemorrhage	1938-46		1947-51	
	Cases	Deaths	Cases	Deaths
Medical	24*	10	6	2
Emergency partial gastrectomy	—	—	4†	0

* Including one case of perforated jejunal ulcer.

† Including one patient, aged 70, operated on three days after closure of the perforation.

In view of the evident tendency for bleeding to recur it would appear that immediate partial gastrectomy is the preferable treatment for perforations associated with or following shortly after haemorrhage; it is likely that it will also give better results for haemorrhage following perforation.

Late Prognosis

The late prognosis has not been studied in all the patients because of the extensive follow-up investigation carried out by Illingworth, Scott, and Jamieson (1946). Their report, however, did not distinguish between gastric and duodenal perforations, and a limited study has therefore been made to determine whether the late prognosis is materially affected by the site of the perforation.

During the period 1938-48, 74 patients diagnosed as having perforated gastric ulcers were treated by surgical closure of the perforation and survived the immediate post-operative period. Their subsequent course was compared with that of the same number of patients who survived the same operation for a perforated duodenal ulcer. The duodenal patients were of the same sex, of the same 10-year age group, and had perforated as closely as possible before or after the corresponding gastric ulcer patients. All were

followed up to the anniversary of their perforations in 1950 or until their ulcers were treated by partial gastrectomy—whichever was the earlier. The period available for follow-up is at least two years in all cases, and extends up to 12 years in some; the result of the method of selection, however, is that the average periods were similar in the two groups, being 6.3 years (S.D. 3.3 years) in the gastric ulcer patients and 6.2 years (S.D. 3.3 years) in the duodenal ulcer patients. Both groups contained the same proportion of men (63/74), and the average ages of the groups were 49.9 years (S.D. 14.8 years) and 49.4 years (S.D. 14.2 years).

The late results of the operation are shown in Table IX. It is seen that the main difference between the prognosis of gastric and that of duodenal patients is that those with

TABLE IX.—Late Results Following Surgical Closure for Perforated Gastric and Duodenal Ulcer

Result	After 2 Years		At Follow-up (i.e., after 2–12 Years)	
	G.U.	D.U.	G.U.	D.U.
Untraced	4	4	6	4
Dead, cause attributed to:				
Peptic ulcer	2	1	3	4
Carcinoma of stomach	6	0	8	0
Other disease	2	3	6*	8†
Total dead	10	4	17	12
Living:				
A. Readmitted for gastric symptoms				
Partial gastrectomy	9	6	15	11
Other gastric operations	3	3	3	7
Medical treatment	8	7	6	6
B. Not readmitted for gastric symptoms				
Recurrence of ulcer pain	13	18	11	14
Occasional mild pain or dyspepsia	7	6	5	5
Symptom-free	19	22	11	15
C. State not known	1	4	—	—
Total living	60	66	51	58
Total cases	74	74	74	74

* Certified causes were cancer of the lung (2), heart failure, broncho-pneumonia, hypertrophy of the prostate, and enemy action.

† Certified causes were pulmonary tuberculosis, cancer of the larynx (an operation for pyloric stenosis had been performed a few months earlier), myocardial degeneration (2), pneumonia, asthma, intestinal obstruction, and chronic nephritis.

perforated "gastric ulcers" have an appreciable risk of dying of carcinoma of the stomach (11% against 0%). The eight cases shown in Table IX as dying of carcinoma of the stomach include seven reported previously (Doll, 1950). The additional case was traced in the course of the present study (Case 1).

Case 1.—A man aged 61 was admitted on July 2, 1946, with a four-months history of abdominal pain, which had been treated elsewhere as being due to a gastric ulcer; for four hours he had had severe epigastric pain of sudden onset. At operation a perforated gastric ulcer 2 in. (5 cm.) in diameter was found low down on the anterior wall of the lesser curvature. The perforation was closed by an omental graft because, "owing to the size of the ulcer and surrounding oedema, stitches could not be inserted." Recovery was uneventful. Gastroscopy on July 24 revealed antral spasm, which prevented a full view being obtained. He was discharged on July 31. Two months later he complained of daily vomiting, and a barium meal showed a large stomach with a 24-hour residue and a deformed duodenal cap. He was readmitted and a partial gastrectomy was performed on September 27. The pylorus was found to be much distorted and thickened from the presence of an "ulcer" on the anterior wall. The stomach was not examined microscopically. He kept well for three years, when he began to complain of lassitude and, at the beginning of March, 1950, of painless jaundice. He was readmitted on April 24, 1950, and died on July 5. At necropsy the remnant of the stomach was healthy. The liver was found to be enlarged and the common bile duct was obstructed by a carcinomatous mass in the porta hepatis. No other growth was found anywhere else in the body. It is presumed that the original antral ulcer was malignant.

Another patient (Case 2) might also be classified as having had a carcinoma of the stomach at the time of perforation, but he has been classified in Table IX among

those patients dying of some disease other than peptic ulcer or carcinoma of the stomach, as the carcinoma is presumed to have been a secondary.

Case 2.—A man aged 60 was admitted on May 22, 1948, with a history of abdominal pains for ten months and severe pain of sudden onset for eight hours. At operation a perforated gastric ulcer was found on the middle third of the greater curvature posteriorly; closure was obtained by oversewing with omentum. He made an uneventful recovery. A barium meal on June 8 showed an irregular ulcer crater in the middle third of the lesser curvature, with the greater curvature drawn in opposite it. Gastroscopy on June 10 showed a mid-gastric contraction ring with some thickening of the mucosa posteriorly; no ulcer was seen and the stomach beyond the constriction was normal. A repeat gastroscopy on July 8 showed no change. He was discharged on July 8 and kept well apart from a cough, which developed at the end of September. In April, 1949, he was admitted to Hillingdon Hospital complaining of pain in the right arm, and on June 4 he died. At necropsy a carcinoma was found in the left lower lobe bronchus with extensive secondaries in the bones, suprarenals, peritoneum, and kidneys. The stomach showed two small chronic lesser-curve gastric ulcers and a small polypoid mass on the greater curvature, "which appeared histologically to be a secondary from an oat-celled carcinoma of the bronchus."

Apart from the greater risk of dying from carcinoma of the stomach following a perforated gastric ulcer, there was little difference between the two groups in the course of the disease during the follow-up period. The outstanding fact was the generally poor prognosis. Of 138 patients followed up, 29 died, including 7—that is, 5% of all the patients—who died of their ulcers. The proportion dying from peptic ulcer is far higher than would be expected to occur in a normal population, and an additional 5% mortality within an average of six years is an important consideration in the assessment of the effects of treatment, when the immediate mortality is as low as it now is.

Of the 109 patients known to have survived at the time of follow-up, 36 (33%) had been subjected to a further gastric operation. In Table X the patients have been sub-

TABLE X.—Late Prognosis among Survivors from Perforated Peptic Ulcers, Subdivided by Sex and Age of Patient, Length of History, and Previous Diagnosis of an Ulcer

Characteristic of Patient	Further Gastric Operation During Follow-up Period		Test of Significance of Difference
	Yes	No	
Sex:			
Males	27 (30%)	64 (70%)	$\chi^2 = 2.808$ $n = 1$ $0.05 < P < 0.10$
Females	9 (50%)	9 (50%)	
Age:			
Under 45	17 (33%)	34 (67%)	$\chi^2 = 0.0040$ $n = 1$ $0.90 < P < 0.95$
45 and over	19 (33%)	39 (67%)	
Length of history:			
1 year or less	7 (18%)	31 (82%)	$\chi^2 = 5.627$ $n = 1$ $0.01 < P < 0.02$
More than 1 year	29 (41%)	42 (59%)	
Previous diagnosis of an ulcer:			
Yes	21 (50%)	21 (50%)	$\chi^2 = 8.899$ $n = 1$ $P < 0.01$
No	15 (22%)	52 (78%)	

divided in a number of ways to see whether it is possible to define simply the class of patient likely to require further operation.

Length of history and diagnosis of the presence of an ulcer before the perforation occurred seem to be the two most useful criteria. Forty-one per cent. (29/71) of the patients who survived and who gave a history of dyspepsia of more than one year and 50% (21/42) of the patients in whom the presence of an ulcer had been proved before the perforation occurred were operated on again during the follow-up period. On the other hand, only 18% (7/38) of the patients who gave a history of dyspepsia of one year or less and 22% (15/67) of those in whom the presence of an ulcer had not been proved before the perforation were re-operated on. The sex and age of the patient did not

give much indication of the subsequent course of the disease, but the number of cases in women was small, and it is possible that a sex difference would be revealed by larger numbers. Looked at from the point of view of freedom from symptoms, similar results are obtained. The sex and age of the patient seem to be unimportant, but 32% (12/38) of the patients with histories of one year or less remained symptom-free against 20% (14/71) of those with longer histories, and 30% (20/67) of those who had not had an ulcer diagnosed previously remained symptom-free, against 14% (6/42) of those who had. It can be concluded that symptoms which had lasted for more than a year or which had been severe enough to result in an ulcer having been already diagnosed before the perforation occurred are indications that the course of the ulcer disease will be unsatisfactory if the perforation is treated by simple closure.

Discussion

In recent years immediately good results have been reported with each of the three main methods of treatment; examples are shown in Table XI. The two series

TABLE XI.—*Immediate Results of Different Methods of Treatment: Recent Series*

Authors	Period of Admission	No. of Cases	No. of Cases Treated by:			General Fatality Rate
			Gastric Aspiration	Surgical Closure	Immediate Partial Gastrectomy	
Taylor (1951) ..	1946-50	73	72	1	0	9.6%
Heslop, Bullough, and Brun (1952)	1947-51	110	104	6		8.2%
"	1946-50	124	20	104	0	9.7%*
Present authors ..	1947-51	340	20	301	19	7.9%
Nuboer (1951) ..	1947-50	65	3	0	62	6.2%
Lowdon (1952) ..	1951	65	1	13	51	6.2%

*Including one death from haematemesis a few days after suture of the perforation, excluded from the fatality rate reported by the authors.

reported by Heslop, Bullough, and Brun are of particular interest for comparative purposes, as the patients were treated in neighbouring hospitals. The authors commented that "the two surgical departments of the hospitals concerned are both engaged in general surgery, are roughly the same size, they receive their patients from the same general practitioners of the area, and one of us is the connecting link between the two hospitals in that he is on the staff of both." The separate fatality rates for the groups of patients selected for the different forms of treatment differ greatly—for example, only one death occurred among the 132 patients treated by immediate partial gastrectomy—but the immediate overall fatality rates are strikingly similar.

In these circumstances conclusive evidence of the superiority of one or other method is likely to be obtained only by means of a controlled trial which, because of the low fatality rate now associated with all forms of treatment, would need to be very extensive. In the published reports the low fatality with immediate partial gastrectomy must be partly due to the selection of good-risk cases for operation, just as the high fatality with medically treated cases is often due to the limitation of the method of treatment to patients who are already moribund. We believe, however, that it may be wrong to consider the three possible methods of treatment as rivals; if the maximum immediate and late benefit to the patients is to be achieved, all three may well have a proper place in every series. In our opinion, tentative conclusions about the indications for each method of treatment are justifiable on the basis of the existing evidence. We assess them as follows.

Medical treatment has not been reported to provide a notably better immediate prognosis than the standard surgical treatment; it does not permit patients to be selected for immediate partial gastrectomy after inspection of the ulcer, and there is no reason to suppose that the late prognosis is any better than that achieved by simple surgical closure.

The method is contraindicated in the presence of bleeding or of pyloric stenosis, for a perforation after heavy eating or drinking, and in air-swallowers. Tanner (1951) sums up as follows: "The non-operative treatment demands frequently repeated expert clinical and radiological assessment, and any error in gastric aspiration, any momentary neglect, any lack of skilful observation, may be followed by disaster for the patient. . . . It is only safe in the hands of the enthusiast with ample medical and nursing assistance and is not suitable for routine usage." The method has been shown to be practicable, and is preferable when: (a) efficient surgery is not readily available; (b) other associated diseases—for example, recent coronary thrombosis—greatly increase the risk of surgery; and (c) perforation has occurred at gastroscopy, when the stomach is empty; for experience has shown that the perforation in this last group is often no longer detectable by the time laparotomy is performed.

Immediate partial gastrectomy has been shown to be a practicable method of treatment, compatible with an excellent immediate prognosis. As most ulcers which perforate acutely are on the anterior wall of the duodenum, the operation is technically easier to perform as an emergency for perforation than for bleeding, when the ulcers are often posterior and penetrating. It is the method of choice for a surgeon experienced in the technique when: (a) the perforation is gastric, and, although the ulcer may appear simple, there is in fact a considerable risk that it may hide an unrecognized carcinoma; (b) the patient gives a history of more than one year's dyspepsia and an ulcer has been diagnosed previously (because a high proportion of such patients will require a further operation if treatment is limited to simple closure); or (c) perforation and haemorrhage from an ulcer occur concomitantly.

We do not think it likely that immediate partial gastrectomy will be shown to be the method of choice for all perforations. It is possible that the immediate prognosis may be even better than that with simple closure of the perforations, by eliminating the deaths due to further complications arising from the persistence of the ulcer; but we have little firm knowledge of the ultimate results, and several reports have suggested that it may predispose to pulmonary tuberculosis (Pulvertaft, 1952). We do not, therefore, think that the operation can be justified as a routine procedure in duodenal ulcer patients in whom the ulcer has never previously been diagnosed and in whom the late prognosis with simple closure is reasonably satisfactory. Particularly is this so when the patients have no memory of prolonged discomfort from their ulcers to set against the symptoms of the dumping syndrome (should they arise).

Surgical closure of the perforation is now a highly satisfactory method of treatment, so far as the immediate prognosis is concerned. It is reasonable to continue to use it in the absence of positive indications for either of the other methods.

Summary

A series of 715 patients with perforated peptic ulcers, admitted during the period 1938-51, is reported.

Since 1947 there does not seem to have been any appreciable change in the fatality rate; in 340 cases, including those undiagnosed till after death, it has been 7.9%. Twenty patients were not operated on, mostly because the condition was not diagnosed or the patient was too ill; 17 died. In 301 patients simple surgical closure was carried out; 10 died, giving a fatality rate of 3.3%. Nineteen patients were treated by immediate partial gastrectomy without a death; in the first six months of 1952 the number so treated has been increased to 30. The concurrent association of haemorrhage and perforation was successfully treated by both simple closure and by immediate partial gastrectomy.

Seventy-four patients treated by simple closure for perforated gastric ulcers and an equal number of com-

parable patients with perforated duodenal ulcers were followed up after two to twelve years. Ten patients could not be traced. Eight (11%) of the "gastric" patients, but none of the "duodenal" patients, are known to have died of carcinoma of the stomach. Seven (5%) of all the patients died of peptic ulcer.

The late prognosis among the known survivors was unaffected by the sex or age of the patients or the site of the ulcer. It was affected by the length of history prior to the perforation and by whether or not the ulcer had been previously diagnosed; in the latter group 50% suffered a further gastric operation.

The advantages and disadvantages of the three current methods of treatment are discussed, and it is concluded that no one method should be the method of choice in all cases. In any one series all three methods have their proper place. Tentative conclusions about the indications for choice of method in individual cases are suggested.

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GRANULOMA OF THE NOSE AND PERIARTERITIS NODOSA

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[WITH SPECIAL PLATE]

From case reports published during the past twenty-one years there gradually emerges the picture of a peculiar syndrome consisting of a chronic ulcerating granulomatous inflammation of the nose, nasal sinuses, and often pharynx, larynx, and trachea, which is followed after a time by generalized periarteritis nodosa, and which leads almost invariably to a fatal issue.

The dominant lesion at the outset of the disease causes a purulent discharge from the nose, which is usually also obstructed. The nasal mucosa presents a characteristic picture of ulcers with yellow crusts which bleed on removal, and necrosis of the bone may appear later. These symptoms are usually accompanied by low-grade fever, and within a few weeks the patient is obviously becoming seriously ill, with albuminuria, signs of renal and cardiac failure, and a rising blood

urea. The terminal illness is usually short, death occurring about six months after the onset of the nasal lesions. Necropsy shows characteristic lesions of periarteritis nodosa in many organs.

This syndrome was first described in 1931 by Klinger (1 case), and since then by Wegener (1939), 3 cases; Lindsay, Aggeler, and Lucia (1944), 1 case; Weinberg (1946), 1 case; and Howells and Friedmann (1950), 1 case. Four of these patients were males and three females; their ages ranged from 23 to 70, and the total duration of illness from six to thirteen months. In all of them the post-mortem findings confirmed the diagnosis.

We record here two cases of this syndrome seen recently. In both of these a diagnosis was made comparatively early in the course of the disease—in the first case on the microscopical appearance of the nasal granuloma, and in the second on account of the striking similarity of the nasal lesions to those seen in the first case.

Case 1

A bus inspector aged 49 was admitted to St. Nicholas Hospital, Plumstead, under the care of Mr. L. E. Gardiner, on June 18, 1951, for investigation of bilateral nasal obstruction, nasal discharge, and an aching pain over the nose of three weeks' duration. There was nothing relevant in his past history, and he had not been given sulphonamides.

Examination showed slight generalized swelling of the nose externally and a thick, blood-stained discharge; the nasal mucosa was widely ulcerated, and had a raw granular surface, covered in parts with a yellow crust. It bled easily when touched; there was no fetor. The patient's general condition was good apart from a slight pyrexia and some malaise. An x-ray film of his nasal sinuses was clear. A course of penicillin injections, 300,000 units daily for 12 days, cleared up the discharge, but did not heal the mucosal ulceration.

A biopsy of the nasal mucosa on June 25 showed appearances interpreted as possibly tuberculous, and an x-ray film of his chest on July 6 revealed tuberculous apical lesions of doubtful activity on the right side. He was given a course of streptomycin, 0.5 g. twice daily, for five weeks, with P.A.S.

Persistent failure to find the tubercle bacillus in the sputum led to revision of the diagnosis, and a further nasal biopsy (Special Plate, Fig. 1) on July 16 was sent to one of us (M.O.S.) and reported on as follows: "The material consists of fragments of granulation tissue containing a fair number of eosinophils, and a small number of multinucleated giant cells of foreign-body type and of Langhans's type. There are no areas of caseation, and no tubercle bacilli have been demonstrated; one cannot at this stage entirely exclude tuberculosis, but the condition this resembles most is not tubercle but the so-called 'giant-cell granuloma of nasal sinuses.' This condition has been reported as a presenting lesion in patients who have subsequently developed periarteritis nodosa."

At the beginning of August the patient developed slight left exophthalmos, and another x-ray film of his sinuses showed left antral infection. Mucopus containing *Staph. pyogenes* and pneumococci was washed out at puncture. Subsequently a muscle biopsy from the thigh showed a small acutely inflamed artery, confirming the diagnosis of periarteritis nodosa (Fig. 2). By the second half of August he had developed gross oedema of the limbs and a peripheral neuritis of the mononeuritis multiplex type. He became severely breathless with left ventricular failure, and a chest x-ray film showed "bat's wing" changes in the mid-zones. Throughout this illness the nasal picture was unchanged.