materially reduce the incidence of painful side-effects. Finally, if the Gambia can be considered as representative of communities in West Africa the hazard of swiftly creating widespread drug resistance in plasmodia through the result of a repository antimalarial in this area would seem to be smaller than has been feared by some authorities.

Summary

The repository antimalarial properties of single doses of cycloguanil pamoate were tested in hyperendemic field conditions in the Gambia, West Africa. The first subgroup of treated subjects developed pain, tenderness, induration, and swelling at the injection site in high incidence, and sterile abscess formation occurred in 27%. Change of injection site to one less closely associated with adipose tissue greatly reduced the incidence of local reaction in subjects treated subsequently. No signs indicative of systemic toxicity were detected in treated or control subjects and haemoglobin concentrations in the former tended to improve after dosage.

Asexual parasitaemia existed in 65% of treated subjects before dosage. At day 7 post therapy all were trophozoite-free, though gametocytaemia persisted. Before injection 63% of control subjects were similarly parasitized and by day 7 55% were still infected.

Chemoprophylaxis following cycloguanil administration was of substantially greater duration than would have been expected to follow a single dose of any known antimalarial. However, compared with results obtained in American volunteers its duration was disappointingly short. It is suggested that the

extreme muscular activity of Gambian subjects may have increased rates of drug absorption and excretion.

The occurrence of strains of plasmodia resistant to cycloguanil, pyrimethamine, or proguanil was not observed during the trial. The absence of signs of systemic toxicity following cycloguanil administration indicates that further field trials should be undertaken at higher dosage levels.

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Perforated Peptic Ulcer in the West of Scotland: a Survey of 5,343 Cases During 1954–63

COLIN MACKAY,* M.B., CH.B., F.R.C.S., F.R.C.S.ED., F.R.C.S.GLASG., B.SC.

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The incidence of perforated peptic ulcer in the West of Scotland has been studied from 1924 until 1953 (Illingworth, Scott, and Jamieson, 1944; Jamieson, 1955). This paper is concerned with the period 1954 to 1963.

As in the previous surveys, the area included the City of Glasgow and the Counties of Argyll, Dunbarton, Lanark, and Renfrew. This is a compact region and forms, surgically speaking, an isolated community. The hospitals in the area handle virtually all the emergencies occurring within the region and very few outside it. The population, which exceeds two million, is mainly industrial, being concentrated around Glasgow and Clydeside. The rural population, which is small, is located mainly in the highland county of Argyll.

The features of a perforated peptic ulcer are usually so dramatic that it was felt that few patients would fail to reach hospital. The study was therefore confined to a search of hospital case records, operation log-books, and post-mortem records. Only those cases in which the perforation was confirmed, either at operation or at necropsy, were included in the survey. The so-called "leaking ulcers" recovering without operation were excluded from the survey, as most clinicians

agree that such a diagnosis is difficult to establish with certainty.

All the hospitals which accept surgical emergencies were included in the survey. The information obtained from the case records was recorded on dual-purpose punch-cards to facilitate the subsequent analysis.

The area studied, the technique used, and the criteria adopted are the same as those in the previous surveys by Illingworth *et al.* (1944) and Jamieson (1955). The results are therefore comparable.

In this paper I wish to consider four aspects of perforated peptic ulcer: (1) the incidence, (2) the time, (3) the site, and (4) the treatment of perforation.

Incidence of Perforation

Fig. 1 shows the incidence of perforation in males and females over the 40-year period 1924–63. There was a fairly steady increase, except for the spike occurring in 1940 and 1941, up until the early 1950's. However, over the past 10 years the incidence has declined. There were 5,343 perforations in the period 1954–63, exactly 1,000 fewer than in the previous decade, and this despite a small increase in the popula-

* Hall Tutorial Fellow, University Department of Surgery, Western Infirmary, Glasgow. Now Registrar in Surgery, Western Infirmary, Glasgow.

tion of the region. Between 1924 and 1953 the population remained fairly constant at about 2.1 million, but over the past decade it has been 2.2 million. From these estimates of population the incidence of perforation per 100,000 can easily be calculated; for example, the incidence per 100,000 was 19 in 1930, 32 in 1950, and 23 in 1960.

FIG. 1.—Incidence of perforation, 1924–63. 1924–53 figures obtained from Jamieson (1955).

This decline in the incidence of perforation in males is explicable in three ways. Firstly, it could be real. Secondly, it might be due to an increasing use of conservative treatment; this is unlikely to be the case, as there has been no definite policy within the region to treat perforations conservatively. The third explanation of the decline could be a reduction in the number of stomachs at risk owing to the number of partial gastrectomies previously performed. This is a possibility, but is unlikely to be the whole explanation. Unfortunately no figures are available of the number of gastrectomies performed in the region over the past 30 years.

In a study of the incidence of perforation in Sweden Norberg (1959) found a slow increase from 1936 to 1950 and thereafter a sharp increase until 1954 and only a slight fall from then until 1957. The rise in incidence was greater than could be accounted for by the increase in the population. Petré (1951) reviewed all the perforations operated on in Sweden during 1930–48, and found that there was a slow rise in incidence from 6.9 per 100,000 population in 1930 to 12.1 in 1948. These figures show a much lower incidence of perforation than that observed in the West of Scotland. Lazarus (1964), in a survey of perforations in Israel, also found a much lower incidence; in the period 1953–8 the incidence was 5 per 100,000 population.

Norberg stated that “stress” was probably the cause of the increase in the incidence of perforation, and suggested that modern therapeutic treatment with drugs such as the corticosteroids and Butazolidin (phenylbutazone) might be partially responsible. In the present survey there were very few patients who perforated while on these drugs. It is unlikely that “tension” and “stress” have decreased to such an extent in the past decade as to explain the fall in incidence of perforation observed in the West of Scotland.

Sex Distribution

The incidence of perforation in males and females is given year by year in Fig. 1, and is summarized by decades in Table I.

TABLE I.—Sex Incidence of Perforation, 1924–63

Period	Males	Females	Ratio
1924–33	3,450	186	19 : 1
1934–43	5,046	276	18 : 1
1944–53	5,854	489	12 : 1
1954–63	4,563	780	6 : 1

It can be seen that the number of perforations in males has fallen in the last decade; in contrast with this the number in females has increased progressively from 186 in 1924–33 to 780 in 1954–63. The male-to-female ratio has therefore fallen steeply from an initial 19:1 to a final 6:1. A similar fall in the male-to-female ratio was reported from Ayrshire (Nisbet, 1964), where the ratio was 14:1 in the period 1951–5 and 8:1 in the ensuing five years.

It is interesting to speculate whether the trend of the past decade will continue and restore the sex incidence of the 1890's. At the end of the nineteenth century and the beginning of the present one perforations were more common in females than in males (Barker, 1896; Brunner, 1903; Jennings, 1940).

Bager (1929), in a survey of perforations in Sweden between 1911 and 1925, found that the number of females remained constant, whereas the number of males showed a steady and marked increase.

Surveys in various countries show a wide range in the percentage of females with perforation. In Austria the figure was 25% (Hienert, 1951), in Israel it was 8.3% (Lazarus, 1964), in Finland it varied from 5.3% (Blomquist and Fock, 1956–7) to 6.5% (Antila, 1964), while in the Moscow district it was as low as 2% (Yudine, 1939).

The above percentages, however, are not all for the same period of time, and it is important to compare sex ratios, from different countries, over the same period. For instance, Antila (1964), in his survey of perforated peptic ulcer in Finland, compares his figure of 6.5% females observed in 1947–61 with the figure of 5% observed in the West of Scotland between 1924 and 1943. The percentage in females in the West of Scotland between 1947 and 1961 was actually 11.2, which is much higher than the Finland percentage for the same period.

This indicates the importance of observing the dimension of time in studies of peptic ulcer, the pattern of which seems to be constantly changing.

Age Distribution

The general features of the age distribution of patients with perforation are shown in Fig. 2. Over the past 10 years, as in the previous surveys, the majority of patients were in the middle-age group. However, in this survey the number was

FIG. 2.—Age distribution of patients with perforation, 1954–63.

greatest in the 50–54-year age group, whereas in the 1944–53 survey it was greatest in the 40–44-year group. There has been a material increase in the mean age of both males and females with perforation over the past 10 years. Compared with the figures for the previous decade the mean age in males has risen from 42.9 to 46.1 years and in females from 44.2 to 50.2 years.

Norberg (1959), in a survey of 1,103 perforations in Sweden in the period 1936–57, found that the peak incidence was in the 30–39-year age group up until 1955, after which the

greatest number was observed in the 40–49-year group. It was felt, however, that this alteration was due mainly to an alteration in the age distribution of the population at risk. Blomquist and Fock (1956–7) found that in Finland the peak incidence was in the 40–49-year age group. Lazarus (1964) found, in a survey of 486 cases in Israel, that the mean age of perforation in males was 46.5 years and in females 45.5 years.

The incidence of perforation in males of varying ages is shown in Fig. 3. From this it is seen that over the past 10 years the incidence has fallen in all age groups except the elderly, where it has actually risen. This may well be due to the fact that ulcer patients are surviving longer.

FIG. 3.—Incidence of perforation in males per 100,000 males living at each five-year age-group. Based on censuses of 1931, 1951, and 1961 and perforation figures for 1930–2, 1950–2, and 1960–2.

The incidence of perforation in males and females rises with age, as is shown in Fig. 4. For instance, in the 20–24-year age group it is 40 per 100,000 in males and 1 per 100,000 in females. The corresponding figures for the 70–74-year age group are 89 and 19 respectively.

FIG. 4.—Incidence of perforation in males and females per 100,000 living at each five-year age group. Based on census figure for 1961 and mean incidence of perforation for 1960, 1961, and 1962.

The rise in the mean age of patients with perforation is probably due to two factors: (1) the higher incidence in the elderly compared with the previous decade, and (2) an increase in the age of the general population of the area, an increase which has been pronounced over the past decade.

Time of Occurrence

Monthly Incidence

Perforations occurring in like months throughout the period 1954–63 were totalled. The totals were adjusted to give values

for a 31-day month in order to render all months comparable, as shown in Table II.

TABLE II.—Monthly Incidence of Perforation, 1954–63. Adjusted Figure Represents a 31-day Month

Month	No. of Perforations		Month	No. of Perforations	
	Actual	Adjusted		Actual	Adjusted
January ..	550	550	August ..	350	350
February ..	451	499	September	338	349
March ..	484	484	October	352	352
April ..	433	447	November	399	412
May ..	481	481	December	565	565
June ..	478	494	Unknown	2	
July ..	460	460			

The peak incidence occurs in December and January. During the spring and early summer the incidence remains more or less constant. There is, however, a dramatic decline in incidence during the months of August, September, and October. This pattern of monthly incidence has remained more or less the same in the West of Scotland for the past 40 years.

It is instructive to analyse in more detail the high incidence seen in December and January. Table III shows the average daily incidence throughout the nine weeks of December and January. It is obvious that there is a fairly marked increase between 22 December and 4 January—that is, during the festive period.

TABLE III.—Average Daily Incidence of Perforation Throughout the Nine Weeks of December and January, 1954–63

Week beginning:	December					January			
	1	8	15	22	29	5	12	19	26
Average daily incidence ..	13	16	17	23	24	18	18	15	16

Webster and Weir (1958), in a survey of perforated peptic ulcer in North-east Scotland, found that the greatest number of perforations occurred in the summer months. Their survey dealt with the Aberdeen area, a tourist centre; it may be that the summer season is the busiest time of the year in that part of Scotland, which may explain the higher incidence of perforation at this time. Absence from Glasgow on holiday might account for some of the decline in August, observed in the present survey, but is certainly not responsible for the low figures of September and October. Nisbet (1964), in a survey of perforations in Ayrshire, found that the greatest number occurred in the January–April period, while the smallest numbers were in September and October.

It may be that this autumnal decline, so marked in the West of Scotland survey over the past 40 years, is a result of the period of rest enjoyed in the summer vacation, though this is of course mere speculation. The increase in incidence over the winter months may be partly due to overwork and fatigue and partly to dietary indiscretion and alcoholic excess, especially over the festive period. An attempt was made in this survey to relate the perforation to the ingestion of alcohol. In 231 patients (4.3%) there was a history of ingestion of alcohol. This is likely to represent the minimum proportion, as in many cases no record would be made of previous alcoholic ingestion in the case notes.

Blomquist and Fock (1956–7) found that the incidence of perforation was highest in South Finland between May and September. Their series was a small one, however. They suggested that as most of their patients were manual workers—for example, farm labourers—the summer was probably the busiest time of the year. The changeable weather was suggested as a cause of the high incidence in the autumn. Cedergren (1924), also in Finland, and Yudine (1939), in Moscow, both found that the peak incidence of perforation occurred in the April–October period.

Daily Incidence

Perforations occurring on like days throughout the 10-year period are shown in Table IV. Perforations occur most commonly on a Friday and least commonly on a Sunday; the difference is not just a slight one, the ratio of Friday to Sunday perforations being greater than 3:2. This pattern of the daily incidence of perforation has remained surprisingly constant for the past 40 years, as shown in Fig. 5. Indeed, the pattern has been exactly the same for the past 20 years.

TABLE IV.—Daily Incidence of Perforation, 1954–63

Day	Male	Female	Total
Sunday	455	84	539
Monday	560	95	655
Tuesday	663	114	777
Wednesday	675	92	767
Thursday	614	113	727
Friday	811	132	943
Saturday	723	118	841
Unknown	62	32	94

FIG. 5.—Daily incidence of perforation, 1924–63.

It was felt that there might well be a difference between males and females in the pattern of daily incidence. However, as Table IV shows, females as well as males perforate most commonly on a Friday and least commonly on a Sunday.

Webster and Weir (1958) found that in North-east Scotland perforations occurred most commonly at the end of the working week and that the incidence fell over the week-end. Nisbet (1964) found that in Ayrshire perforations were most common on a Thursday and least common on a Sunday.

It would appear, therefore, that the Scottish Sabbath is still a day of rest, at least so far as perforations are concerned. It is interesting that Lazarus (1964), in a survey of perforations in Israel, found that the incidence was lowest on a Saturday, the Jewish Sabbath.

The high incidence observed in the present survey on Fridays and Saturdays may or may not be due to the effects of a busy working-week. Friday is pay-day for most of the workers in the region, and Friday and Saturday evenings are by far the busiest times of the week so far as alcoholic consumption is concerned. This may or may not explain the high incidence of perforation on these days. The fact that Monday is the second least common day for perforation in the West of Scotland may be due to the effect of rest over the week-end.

Blomquist and Fock (1956–7), in Finland, found that there was a tendency for the number of perforations to increase towards the end of the week. Saxholm (1946), in Norway, found that the majority of perforations occurred on a Saturday, and Korttila (1949), again in Finland, found that Friday was the commonest day; their series, however, were small.

Time of Day

Perforation of a peptic ulcer is usually so sudden that the actual time of occurrence can be ascertained, though unfor-

tunately it is not always recorded. In a search of 5,343 case records the time of occurrence was found in 3,632—that is, approximately two-thirds.

The diurnal pattern of the incidence of perforation in males and females is shown in Fig. 6. In males perforation is relatively uncommon during the night; the incidence rises to a minor peak in the late morning, to a major peak in the late afternoon, and then drops to a lower but stable level till midnight. There is a fall in the incidence after 1 p.m. and 6 p.m., which mark the usual times of meals. There are no corresponding fluctuations of incidence in females, although of course the numbers are smaller.

FIG. 6.—Incidence of perforation in males and females at each hour of the day, 1954–63.

The diurnal patterns of incidence in this and in the previous surveys are closely similar. It may be that the rising incidence throughout the working-day is attributable to increasing fatigue, with the brief drop in incidence during the early afternoon attributable to the lunch-time period of rest. Again, it may be that the incidence of perforation increases with prolonged fasting and drops at the times of the midday and evening meals.

Webster and Weir (1958), in a very small series, found the peak incidence at noon, 5 p.m., and 8 to 9 p.m.—that is, a similar pattern to that in the present series. Most other workers have found that perforations tend to occur towards the end of the working-day. Blomquist and Fock (1956–7) found the peak incidence to be between 3 and 4 p.m., Yudine (1939) between 2 and 5 p.m., and Saxholm (1946) at 5 p.m.

Site of Perforation

In the present survey perforations were classified under the following headings: (a) gastric, (b) pyloroduodenal, (c) stomal, and (d) miscellaneous—for example, oesophageal, Meckel's diverticulum. The term "pyloroduodenal" was used because of the difficulty in differentiating duodenal from juxtapyloric gastric ulcers at the time of operation. The presence of fibrin and oedema may so obscure the situation of the pylorus as to make the differentiation impossible. Table V shows the relative incidence of each type of perforation.

TABLE V.—Site of Perforation, 1954–63

Site	Total	Percentage
Gastric	426	8
Pyloroduodenal	4,795	90
Stomal	106	2
Miscellaneous	3	0
Not recorded	13	0

Pyloroduodenal ulcers are still by far the commonest sites of perforation. However, it is instructive to note the ratio of pyloroduodenal to gastric perforations over the past 40 years (Table VI).

TABLE VI.—Ratio of Pyloroduodenal to Gastric Perforations, 1924–63

Period	Pyloroduodenal Perforations	Gastric Perforations	Ratio
1924–43	3,220	493	6.5 : 1
1944–53	5,503	319	17 : 1
1954–63	4,795	426	11 : 1

There has been a significant alteration in the pyloroduodenal-gastric perforation ratio over the past 10 years. Gastric perforation is now becoming relatively more common. Gastric ulcers were more common than duodenal at the end of the nineteenth century (Barker, 1896; Jennings, 1940); it is interesting to speculate whether or not we are returning to this former state of affairs.

Antila (1964), in his survey of perforated peptic ulcer in Finland between 1947 and 1961, found that 40.4% of perforations were in gastric ulcers. Norberg (1959), in Sweden, found that between 1936 and 1957 22.6% of perforations were in gastric ulcers. These estimates are much higher than ours in the West of Scotland—namely, 5% for 1944–53 and 8% for 1954–63.

It appears, therefore, that although gastric perforations are becoming more common in Scotland they are still much rarer than in Scandinavia. In Israel the ratio of pyloroduodenal to gastric perforations is similar to that found in the West of Scotland. Lazarus (1964), in his survey of the 1953–8 period, found that 91% of perforations were in pyloroduodenal ulcers and 6% in gastric ulcers.

There is a marked difference between the sexes as regards the site of perforation (Table VII).

TABLE VII.—Ratio of Pyloroduodenal to Gastric Perforations in Males and Females, 1954–63

Sex	Pyloroduodenal	Gastric	Ratio
Male	4,182	275	15 : 1
Female	613	151	4 : 1

Though more perforated gastric ulcers are seen in males than in females, gastric perforations are, relatively speaking, much more common in females. This marked sex difference was also observed in the previous survey (Jamieson, 1955), where the pyloroduodenal:gastric ratio was 21:1 for males and 5:1 for females. In Israel the ratio was 16:1 for males and 8:1 for females (Lazarus, 1964).

Site and Age.—There is a fairly wide difference between pyloroduodenal and gastric perforations so far as the age of the patient is concerned. In the present survey the mean age of patients with pyloroduodenal perforations was 46.13 years, whereas with gastric perforations it was 51.18 years.

Treatment

Treatment given to patients in the series is shown in Table VIII. It is evident that simple closure of the perforation was the standard method of treatment. Gastro-enterostomy or pyloroplasty was rarely added. Immediate gastrectomy was resorted to more rarely still. Finally, in a group of about 5%

of patients no operation was attempted, most often because these patients were moribund on admission to hospital.

TABLE VIII.—Treatment of Perforated Peptic Ulcer, 1954–63

Treatment	No.	Percentage
Simple closure	4,726	88.4
Closure and anastomosis	198	3.7
Resection	103	1.9
No operation	282	5.3
Miscellaneous	16	0.3
Not recorded	18	0.4

Summary

Information is presented on the incidence of perforated peptic ulcer in the West of Scotland from 1954 to 1963, thus bringing up to date a survey started from 1924.

The incidence has declined in the past decade. Although there is still a marked preponderance of males, the actual number of females with perforation has increased.

The mean age of patients with perforation has risen in both males and females and is higher in the latter. In elderly people there has been a rise in the incidence of perforation, whereas in all other age groups the incidence has fallen.

Perforations occur most commonly between 5 and 6 p.m., on Fridays and Saturdays, and in December and January. They occur least commonly during the night, on Sundays, and in August, September, and October.

Pyloroduodenal ulcers are still the commonest sites of perforation, but the proportion of gastric perforations has increased over the past decade.

Patients with gastric perforation tend to be older than patients with pyloroduodenal perforation.

Finally, closure remains by far the commonest method of treatment.

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