

Perforated peptic ulcer over 56 years. Time trends in patients and disease characteristics

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Abstract

Perforated gastroduodenal ulcer was studied in 1483 patients in the Bergen area during the years 1935-90 to discover time trends in age and sex, disease characteristics, treatment, and outcome. The male:female ratio fell from 10:1 to 1.5:1, median age increased from 41 to 62 years. Most perforations were found in the duodenum in 1935-64, and in the pyloric and praepyloric area in 1965-90. There was a 10% occurrence of gastric ulcers throughout the study period. Ulcer site was related to age (more gastric and less duodenal perforations with increasing age) and sex (more pyloric and less duodenal ulcers among women). There were twice as many perforations in the evening compared with the early morning. The diurnal variation was more pronounced for duodenal and pyloric than for gastric and praepyloric perforations. Circadian and seasonal variation of ulcer perforation did not change during the 56 years studied. Treatment delay increased from median five hours to median nine hours. Infective complications and mortality fell with the introduction of antibiotics around 1950. General complications has increased in recent years because of the increase of elderly patients. Among patients who died, the proportion with associated disease rose from 27 to 85% during the study period.

(Gut 1993; 34: 1666-1671)

Mr Crisp's description of perforated ulcer from 1843¹ would fit into any modern textbook as far as symptomatology is concerned. From the available published works it can be deduced that the medical management, disease characteristics, and patient characteristics of perforated ulcer have changed since then.²⁻¹¹ To understand these changes it is important that confounding factors related to the geographical and hospital setting are kept constant and that the illness is studied over an extended period of time. This type of study has not been reported in recent publications.

This study describes the changing characteristics of perforated peptic ulcer in a well defined area on the west coast of Norway from 1935 to 1990 based on information from case notes. This offers a unique opportunity to investigate time trends in the patient population, disease characteristics (with detailed site classification), and aspects of management and outcome.

Patients and methods

A total of 1483 patients with acute perforated ulcer admitted to hospital in Bergen catchment area were studied. Patients were identified by

several methods to achieve a complete registration based on computerised (1973-90) and manual (1935-72) recording systems. Case notes were identified based on diagnosis as well as surgical procedure for the years 1973-90. For the years 1935-72 a card system based on diagnosis as well as consecutive recordings of the diagnosis of admitted or operated patients, or both were used for identification of patients. One thousand two hundred and thirty patients were treated at Haukeland hospital, 151 patients at the Deaconess hospital, 70 patients at Betanien hospital, and 32 patients at Red Cross and Florida hospitals.

For the 1296 patients treated at Haukeland and the Deaconess hospital (group I) the following information was obtained from case notes: patient characteristics, previous ulcer history, time of perforation, admittance and operation, preoperative diagnostic procedures, treatment, complications, and death. Information on location of the ulcer was obtained from operation notes as reported by the surgeon and examination of histological specimen(s) if available. For the remaining 191 patients (group II) information on patient characteristics, ulcer location, and operation performed was obtained from consecutive recordings of admitted and operated patients (protocols listing patient data, diagnosis, and date of admittance/operation). Analyses concerning sex, age, and type of operation were performed on data for all patients, the remaining analyses were carried out based on information for patients in group I.

STATISTICAL ANALYSIS

The data were analysed using the statistical program package BMDP¹² on a personal computer. Analyses were based on contingency tables and included simple χ^2 testing and tests for linear trend (P4F) to which the p values in the text refer. Stepwise logistic analysis (PLR) was performed in a forward stepping manner with ulcer site as the dependent variable and sex, age, and year of performance as independent variables. Four analyses were performed, one for each anatomic location compared with the other three. The Tables show the confidence intervals and p values estimated from the final models.

Results

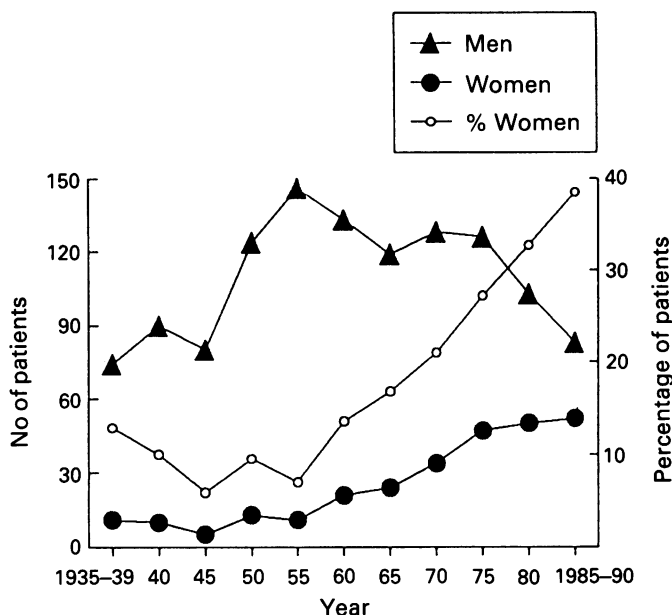
PATIENTS AND CHARACTERISTICS OF DISEASE

Sex and age

Figure 1 shows the number of patients treated and the proportion of women in each five year period. The proportion of women increased

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Year	Men (1205)	Women (278)	Total (1483)
1935-39	74	11	85
40	90	10	100
45	80	5	85
50	124	13	137
55	146	11	157
60	132	21	154
65	119	24	143
70	128	34	162
75	126	47	173
80	103	50	153
1985-90	83	52	135

Figure 1: Number of men and women and proportion of women with perforated ulcer in five year periods from 1935 to 1990.

fourfold during the second half of the study period ($p < 0.001$; linear trend). Median age increased from 38 years in 1935-44 to 60 years in 1985-90 for men, and from 55 years to 69 years for women (positive linear trend: $p < 0.001$ for both sexes).

Ulcer site

Figure 2 shows changes in ulcer location during the study period. The proportion of perforations located in the duodenum decreased from 80 to 42% over the first 30 years and remained stable thereafter. Pyloric ulcers (perforations situated in the pyloric orifice) were uncommon in the first 15-20 years, but increased during the years 1950-65. During the last 25 years the proportion

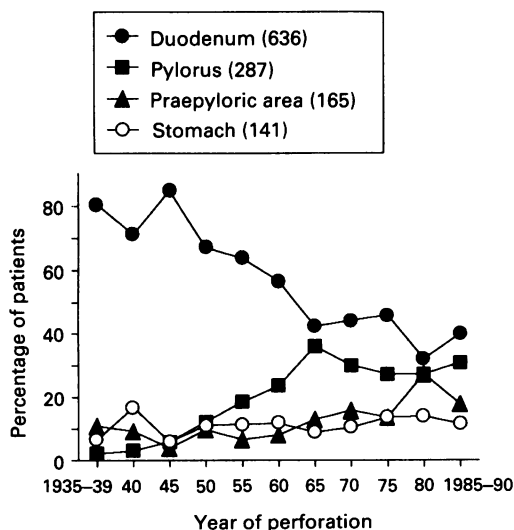


Figure 2: Site of perforated ulcer in five year periods from 1935 to 1990 (n=1229).

of pyloric ulcers has been approximately 30%. There were 5-10% praepyloric ulcers (perforations located within 2 cm proximal of the pylorus) during the first 30 years, after which the proportion increased gradually. Approximately 10% of the ulcers were located in the antrum, corpus or fundus ('gastric ulcers') throughout the study period.

Figure 3 shows the relation between age and ulcer site. With increasing age the number of duodenal perforations decreased while the number of gastric perforations increased. Figure 4 gives location of ulcer for men and women. Women had comparatively more pyloric and less duodenal perforations than men.

Table I summarises the comparative importance of age, sex, and time period for each ulcer site. The final models fitted the data well with p values for goodness of fit of > 0.1 . Adjusting for changes in age and sex distribution, there was a significant time trend for all ulcer types except gastric perforations. Duodenal perforations decreased while pyloric and praepyloric perforations increased during the study period. Duodenal and gastric perforations were related to age; duodenal ulcer affected the younger patients, gastric ulcer the older. There was a true sex difference for duodenal and pyloric perforations, pyloric perforations occurring comparatively more often in women and duodenal perforations in men. There was no sex difference in gastric perforations when adjusting for age. Similarly, pyloric and praepyloric ulcers were not related to age when adjusting for year of diagnosis.

Circadian variation

Figure 5A shows the circadian variation of ulcer perforation. There were twice as many perforations per hour in the evening compared with the early morning. Figure 5B shows the differences in diurnal variation according to ulcer location. For praepyloric and gastric ulcer, relatively more perforations occurred before 10 am than for pyloric and duodenal ulcer ($p = 0.02$). The patterns were similar for duodenal and pyloric ulcers, as well as for praepyloric and gastric ulcers. The circadian variation did not change during the study period (Fig 5C).

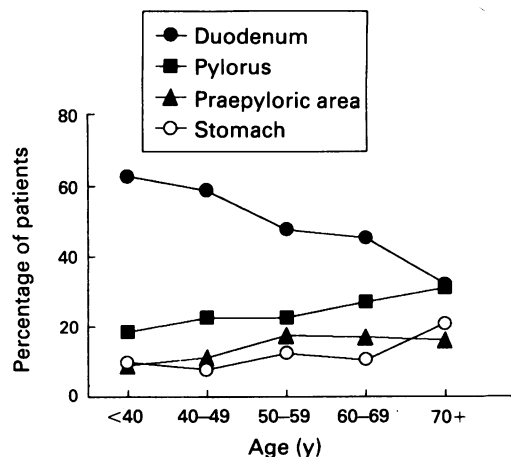


Figure 3: Frequency distribution of perforated ulcer according to ulcer location and age.

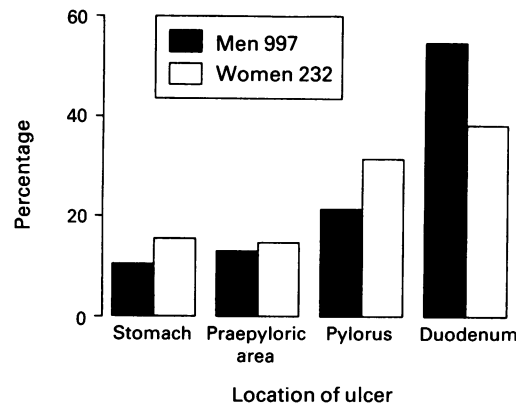


Figure 4: Frequency distribution of perforated ulcer according to ulcer location for men and women.

Seasonal variation

Figure 6A illustrates the seasonal variation. More perforations occurred in early summer (May, June, July) and early winter (November, December). This pattern was mainly caused by the high proportion of duodenal and pyloric ulcers. Gastric and praepyloric ulcers did not show a clear seasonal variation (Fig 6B). The seasonal variation did not change during the study period (data not given).

Previous dyspepsia

Of 1146 patients with available data, 75% had had dyspepsia for more than one month before perforation. For the remaining 25% perforation was the first presentation of ulcer disease. This finding was consistent throughout the study period irrespective of ulcer site. A larger proportion of women had perforation without previous dyspepsia (28% v 18%; p=0.01; analysis of patients admitted 1970–90). Age was not significantly associated to previous dyspepsia (1970–90).

Treatment delay

Treatment delay, defined as time from perforation to operation, increased during the study period (linear trend: p<0.001, n=1128), also for the most recent five year period. The increase was mainly caused by increased in hospital delay (time from hospital admission to operation), while preadmission delay (time from perforation to admission) did not change significantly.

TABLE I Effect of year of diagnosis, age, and sex on distribution of ulcer locations

	Duodenum (n=592) OR* (95% CI)†	Pylorus (n=286) OR* (95% CI)†	Praepyloric area (n=165) OR* (95% CI)†	Stomach (n=141) OR* (95% CI)†
Year:				
1935–54	1	1	1	‡
1955–74	0.41 (0.29 to 0.58)	5.22 (3.03 to 8.98)	1.32 (0.78 to 2.23)	
1975–90	0.31 (0.21 to 0.46)	5.13 (2.95 to 8.94)	2.54 (1.53 to 4.21)	
Age (y):				
<43	1	‡	‡	1
43–58	0.80 (0.60 to 1.07)			0.88 (0.55 to 1.39)
>58	0.56 (0.41 to 0.76)			2.54 (1.53 to 4.21)
Sex:				
Men	1	1	‡	‡
Women	0.67 (0.50 to 0.92)	1.46 (1.05 to 2.03)		

*OR=odds ratio obtained from logistic regression analyses; †CI=confidence intervals obtained from logistic regression analyses; ‡variable was non-significant and not included in final model (p>0.05).

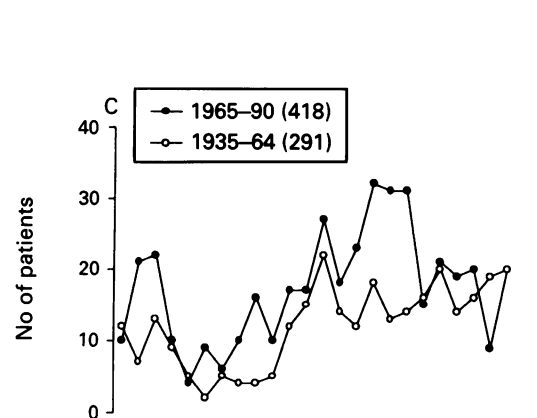
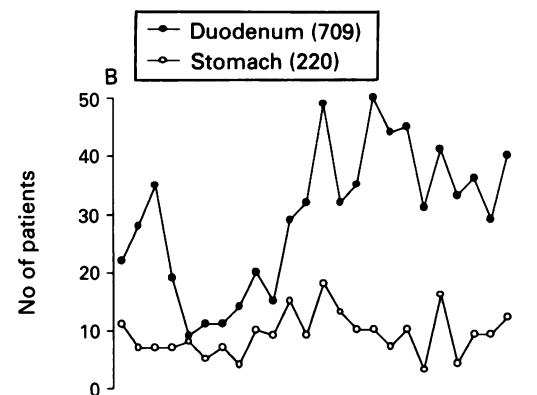
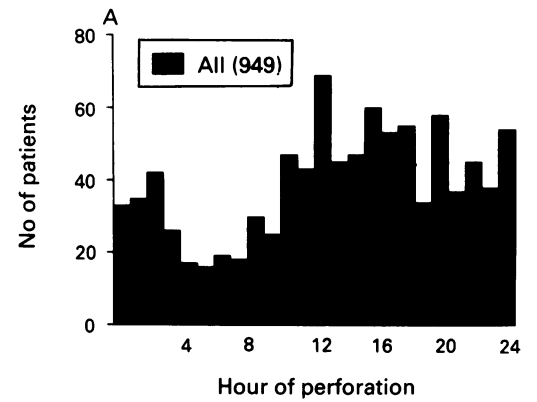


Figure 5: Circadian variation in ulcer perforation for (A) all patients, (B) according to ulcer location ('duodenum' = duodenum + pylorus, 'stomach' = praepyloric area + stomach), and (C) after year of perforation (duodenal + pyloric ulcers). Data from patients with delay <24 hours.

TREATMENT AND OUTCOME

Operations

Figure 7 shows the operations performed for perforated ulcer. Of 1397 cases with available data, 1367 patients (98%) had surgery. During the first five year period, similar proportions of patients had either suture, Billroth II type resection or suture plus gastroenterostomy. From 1940–60 resection was performed in about two thirds, the rest had a simple suture. Over the next 10 years treatment preference changed in favour of simple suture, which has been performed on nearly all patients since 1970. Only 26 patients (2%) were treated conservatively during the 56 year period. Seven patients had no treatment as the final diagnosis was made first at

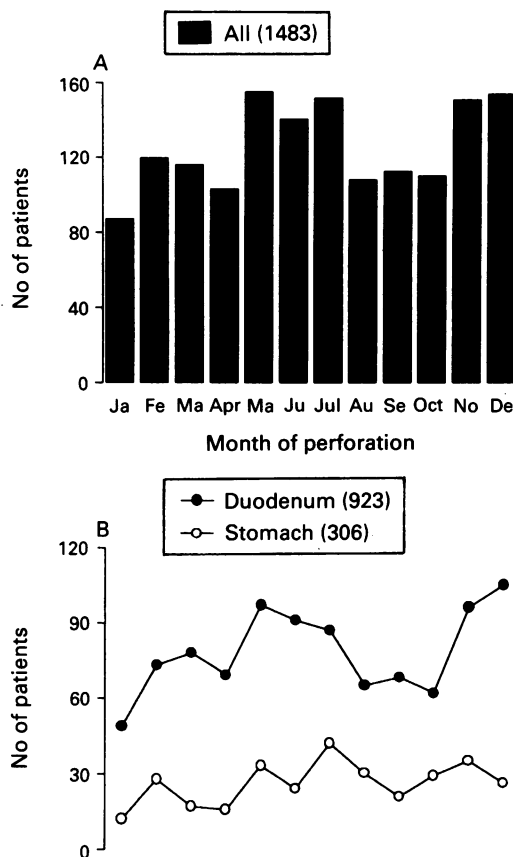


Figure 6: Seasonal variation in ulcer perforation for (A) all patients and (B) according to ulcer location ('duodenum' = duodenum + pylorus, 'stomach' = praepyloric area + stomach). Numbers adjusted to 31 days/months.

postmortem examination, and eight patients died without treatment being started because of poor general condition. Of all patients, 75% were operated outside regular working hours (8 am–4 pm).

Antibiotics

Antibiotics were introduced for the treatment of perforated ulcer in the late 'forties, and have been used in nearly all patients since 1950 (Fig 8).

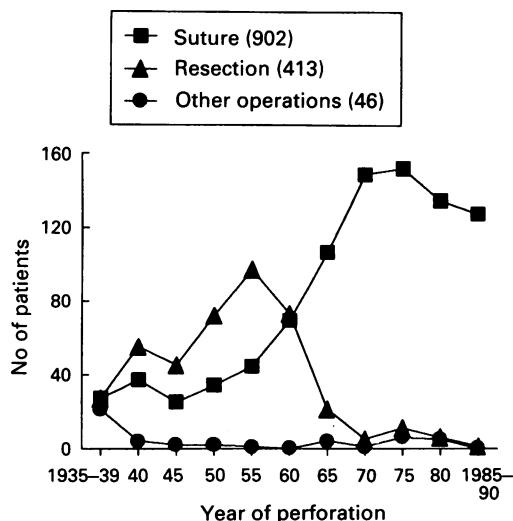


Figure 7: Operations for perforated ulcer 1935–1990 (other operations include suture + gastroenterostomy).

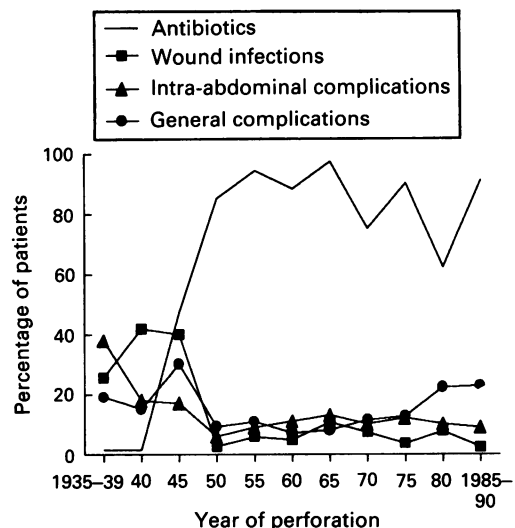


Figure 8: Complication rates (n=1192) and use of antibiotics (n=984) for patients with ulcer perforation 1935–1990.

Postoperative complications

Out of 1241 patients in group I who had surgery, data on complications were missing for 50. Four patients died intra or immediately postoperatively. Of the rest, 334 patients (28%) experienced one or more postoperative complication. Wound infections occurred in 113 patients (10%), 143 patients (13%) had intra-abdominal abscesses or other abdominal complications such as anastomotic leakage, duodenal fistulas, peritonitis or bleeding. General complications (heart and respiratory problems) occurred in 169 patients (14%). Forty three patients (4%) had another operation during the primary hospital stay because of bleeding, fistulas, gastric retention or abscesses.

Figure 8 shows time trends in postoperative complication rates. There was a high incidence of infective complications before 1950. In recent years the frequency of general complications increased. Elderly patients (>50 years) had more complications than younger patients (p=0.005), but no significant sex difference could be found (p=0.4). Ulcers located in the stomach carried a higher complication rate than duodenal, pyloric, and praepyloric ulcers (p=0.01; Table II).

Deaths

One hundred and one patients (8%) died after perforation and related complications. Mortality decreased during the first part of the study period (1935–49), was comparatively stable during the years 1950–80, and increased in the last 10 years. Median age for the patients who died was 67 v 50 years for the total patient

TABLE II Outcome of ulcer perforation by ulcer site*

Ulcer Site	Complications % (n)	Mortality % (n)	Hospital stay median days
Duodenum (n=244)	24.6 (57)	7.8 (19)	7
Pylorus (n=171)	24.1 (41)	7.0 (12)	8
Praepyloric area (n=109)	24.5 (26)	2.8 (3)	8
Stomach (n=74)	38.6 (27)	17.6 (13)	9

*Data from 1970–90.

population. The median age for death increased gradually from 50 years in 1935–44 to 78 years in 1985–90. Gastric ulcers carried a higher death rate than praepyloric, pyloric, and duodenal perforations ($p < 0.001$; Table II).

Of the patients who died, 47 patients (47%) had concomitant serious disease(s) at the time of perforation. Among the patients who died the proportion with associated severe disease increased from 27% in 1935–44 to 85% in 1985–90 (linear trend: $p < 0.001$).

Hospital stay

Time spent in hospital decreased steadily during our study period (linear trend: $p < 0.001$). During the first 10 years, 75% of the patients spent more than two weeks in hospital, in 1985–90 49% were discharged within seven days. Median stay in hospital for the whole period was 11 days. Women and elderly patients spent longer time in hospital than men and younger patients ($p < 0.001$ and $p < 0.001$; data from 1970–90). Patients with ulcer located in the duodenum spent less time in hospital than patients with pyloric, praepyloric or gastric ulcer ($p = 0.001$; Table II, data from 1970–90).

Discussion

Mr Crisp's series¹ consisted of 78% women of median age between 15 and 20 years. A 100 years later (1935–44) 89% of the patients affected by perforated ulcer were men of median age 40 years. Today (1985–90) there are 39% women of median age 69 years. These changes in age and sex are consistent with other reports from the Western world on ulcer perforation^{4-7 10 11 13} and ulcer disease in general.¹⁴⁻¹⁶

Major changes in the location of perforated ulcer have also been seen. In Mr Crisp's series there were 70% gastric ulcers of which half were close to the cardia. A 100 years later, such ulcers were rare and several authors reported that most perforations were located in the duodenum.^{5 6 17} This study shows that over the last 10 years (1980–90) pyloric and praepyloric perforations, encountered rarely decades ago, have exceeded duodenal perforations. It is remarkable that the proportion of gastric ulcer has remained stable over 56 years, particularly when considering the potential impact of ulcerogenic drugs.¹⁸

There are large variations in the published works as to ulcer site.^{4-11 13 17 19-23} Pyloric and praepyloric ulcers are rarely specified as separate groups. This was a minor problem in former days as pyloric ulcers were rare,^{1 5 17} but today this site represents a substantial number.²⁴⁻²⁶ Some authors claim that site classification is impossible as a precise anatomic distinction is difficult to assess because of inflammation. We have classified the perforations based on the surgeon's description, and argue that misclassification is probably not the reason for the time trends shown in Figure 2. The distinction is important as the four ulcer sites differ not only with regard to time trends, but also in patient characteristics, seasonal and circadian variation, treatment, and outcome (Figs 5 and 6; Tables I and II). No other study gives comparable information.

The diurnal pattern of ulcer perforation is remarkably constant irrespective of period of time or geographical setting.^{5-7 10 11 17} Our study disclosed a clear diurnal variation for perforation of duodenal ulcers, much less so for perforation of gastric ulcers. This may be related to variations between the ulcer sites in basic physiological mechanisms, while the stability in diurnal variation of duodenal perforation over time shows that these mechanisms are the same today as they were 50 years ago.

The issue of seasonal variation of ulcer perforation was first reported in 1903² but is still controversial. Several studies^{2 5-8 22} point to an increased perforation rate in early summer and a decrease during the late summer consistent with our findings. Other reports differ entirely from ours^{21 27 28} or claim that there are no seasonal effects at all.^{11 29} Differences in ulcer site may partly explain discrepancies in published works, while geographical differences cannot easily be detected.²⁸ The patterns within defined geographical areas, however, are strikingly similar over different periods of time consistent with our findings.⁵⁻⁷

The stability of seasonal variation for duodenal ulcer throughout the study period makes an interesting historical experiment: dietary factors that were related to seasons in former days but not today, probably do not cause duodenal ulcer perforation. Some reports^{30 31} propose an effect of salt on gastric ulcer but not on duodenal ulcer. Salted food was strongly related to seasons previously, but not after refrigerators and deep freezers became widely used. Thus, a causal relation between salt and duodenal ulcer does not seem plausible. Fresh fruit was seasonal until recent years, and our historical experiment suggests that related dietary factors can largely be excluded as causes of duodenal ulcer.

The increase in treatment delay from 1935 to 1990 in our study seems to be part of a general trend, as older publications report considerably shorter delays^{5 6 8 20} than recent ones.^{24 26 32 33} Factors associated with delay have been analysed for a subpopulation in a previously published paper.³⁴ The development is alarming, and comparable studies should be carried out at other hospitals and for other emergencies.

Outcome of ulcer perforation in terms of complication rates and death improved considerably and was simultaneous with the introduction of antibiotics. Two other studies give data on death from perforated ulcer during the period studied. Both saw a decline around 1950,^{6 11} which can probably be attributed to the introduction of antibiotics.

In former days ulcer perforation could be fatal for otherwise healthy subjects. Today most deaths occur when patients have concomitant serious illness. We cannot find similar time-trend investigations in other published works. In Lanng's study from 1975–84,³⁵ however, 79% of those who died had serious concurrent disease, consistent with 70% during the last 15 years of our study.

The slight increase in death and complication rates during the last years of the study can largely be ascribed to patients being older and generally

more ill. Age has been an important risk factor during all these years.³⁶ Median age of those who died (28 years) has increased more than that of the total patient population (21 years), which indicates that age is an even more important risk factor today. A detailed study of factors influencing death has been published previously for a subgroup of this study population.³⁶

Profound changes have been seen in perforated peptic ulcers in relation to ulcer site, age, and sex of the patients. Seasonal and circadian variation as well as proportion of gastric ulcers did not change during the study period. Treatment results have improved over 56 years in terms of reduced hospital stay, reduced mortality, and complication rates (taking age into consideration) and death now occurring almost exclusively in older patients with concomitant diseases. Despite vast investments in the organisation of health care, preadmission delay (attributed to primary health care and transportation) has not decreased, whereas in-hospital delay continues to increase.

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