Chronic gastritis and gastroduodenal ulcer: a case control study on risk of coexisting duodenal or gastric ulcer in patients with gastritis

P SIPPONEN, K SEPPÄLÄ, M ÄÄRYNEN, T HELSKE, AND P KETTUNEN

From the Department of Pathology and Internal Medicine, Jorvi Hospital, Espoo, District Hospital of Kuusankoski, Kuusankoski, and Second Department of Medicine, University of Helsinki, Helsinki, Finland

SUMMARY Chronic (atrophic) gastritis (AG) is common in active duodenal (DU) and gastric ulcer (GU) disease. In this case control study in consecutive prospective outpatients (571 cases and 1074 controls) who had undergone diagnostic upper gastrointestinal endoscopy and routine biopsies from both antral and body mucosa, we calculated the risk of coexisting active DU and/or GU in different gastritis of the antrum or body and according to grade (superficial gastritis, mild, moderate or severe atrophic gastritis). The risk of coexisting active gastroduodenal ulcer (ulcer in duodenum and/or stomach), as well as the risk of DU or GU, was dependent upon the presence and grade of gastritis in antrum and body mucosa. The risk of coexisting ulcer, as expressed as an age adjusted relative risk (RR) and calculated as odds ratio of gastritis in cases and controls, was significantly increased in the presence of superficial antral and body gastritis (RR=8.5 (7.0-20.0) in men; RR=5.8 (3.3-10.2) in women), as compared with the risk of ulcer in subjects with histologically normal mucosa (RR=1). The risk of ulcer, and the risk of GU in particular, increased further with increasing severity of antral gastritis. In such patients with moderate or severe atrophic antral gastritis the RR of coexisting ulcer even exceeded 20 in men and 10 in women (RR=25.6 (9.0-72.7) in men; RR=11.7 (5.9-23.0) in women). On the other hand, the RR of ulcer, and the RR of DU in particular, was below 1 in the presence of atrophic gastritis in the gastric body, irrespective of the grade of gastritis in the antrum. We conclude that the type and grade of gastritis strongly predicts the risk of coexisting peptic ulcer, and that the risk of coexisting DU or GU increases with an increase in grade of AG of the antrum but decreases with an increase in grade of AG of the gastric body.

Chronic (atrophic) gastritis is common in active peptic ulcer disease. Antral gastritis occurs in 75-95% of patients with duodenal ulcer (DU) and nearly always in patients with gastric ulcer (GU).¹⁻⁹ Although the causal relationship between gastritis and ulcer diseases is unclear and controversial, gastritis may play a role in the pathogenesis of DU and GU diseases and may impair the resistance of the gastric mucosa and consequently increase the risk of ulcer.¹⁰ On the other hand, atrophic gastritis in the gastric body has a negative effect on acid and pepsin secretion, and may subsequently decrease the risk of subjects to contract an active ulcer.¹¹

Gastritis is also common in the general population. It progresses in grade and prevalence with increasing

age,¹²⁻¹⁴ and occurs as different topographic types - that is, as different combinations (phenotypes) of grade and extent of inflammation and atrophy of antral and body mucosa.¹³⁻¹⁸ Little is known about the relationship between peptic ulcer and different types or grades of gastritis. Based on case control design and on consecutive endoscopic series of outpatients with active DU or GU and non-ulcer controls, we calculated the mean risks of coexisting ulcer in patients showing different grades and types of gastritis.

Methods

PATIENTS

The patient series (cases) consists of 571 patients with endoscopically verified active ulcer in duodenum and/or stomach. The series was consecutively and

Address for correspondence: Dr P Sipponen, Department of Pathology, Jorvi Hospital, SF-02740 Espoo, Finland.

Accepted for publication 28 November 1988.

prospectively collected from outpatients who underwent routine diagnostic upper gastrointestinal endoscopy in 1982–1985 in Jorvi Hospital (Espoo), Kuusankoski District Hospital (Kuusankoski) and a private clinic (Endoskopia OY; Helsinki, Finland). All patients underwent gastroscopy with routine multiple biopsy specimens from antrum and body. High quality, well oriented specimens from both sites were available in 489 (86%) patients, and only from antrum or body in 59 (10%) and 23 (4%) cases, respectively. Patients with gastric cancer or patients with ulcer in the cardiac region of the stomach were excluded, as were also patients who had ulcer scars without an active ulcer. Correspondingly, patients with superficial ulcerations, such as erosions or acute mucosal lesions without ulcer, were excluded from the patient series but were included in the control series.

The distribution of the patients of the ulcer series according to age, sex and site of the ulcer (the most proximal ulcer in cases with two or more ulcers) are presented in Tables 1 and 2. Ulcer was multiple (two or more ulcers) in 91 (16%) cases.

CONTROLS

The control series consists of a prospective sample of 1074 non-ulcer patients from the same sources as the ulcer patients, collected consecutively in 1985. Patients with gastric cancer or ulcer scars were excluded from the control series. The controls were endoscoped as for the ulcer patients. High quality, well oriented biopsy specimens from both sites were

available in 996 (93%) cases, only from the antrum in 42 (4%) cases and only from the body in 36 (3%) cases. The distribution of the controls into men and women and into different age groups is presented in Table 3.

INTERPRETATION OF CHRONIC GASTRITIS

Chronic (atrophic) gastritis in antrum and body was interpreted from endoscopic biopsy specimens by using the histological criteria originally presented by Schindler¹² and modified by Siurala *et al*.^{13,14} The criteria correspond with those published by other authors.¹⁵ The grading was done by one of the authors (PS), as follows: normal (N): normal mucosa. No inflammation, no atrophy; superficial chronic gastritis (S): chronic inflammation without loss of normal glands; mild, moderate or severe (total atrophy) atrophic gastritis (A1, A2, A3, respectively); mild, moderate or severe (total) loss of normal glands; varying degrees of inflammation and metaplasias.

Chronic gastritis has been shown to be an age dependent, progressive process.^{16–18} It begins as a superficial gastritis and progresses stepwise from grade to grade, similar in the antrum and body, and among men and women.^{16–18} Different grades of gastritis are well related to function of the stomach – for example, to acid secretion, serum pepsinogen or gastrin levels.¹¹

Examples of the different degrees of antral and body gastritis are presented and illustrated elsewhere.¹⁴

STATISTICAL ANALYSIS

The risk of coexisting gastroduodenal ulcer in different grades and types of gastritis was expressed as a relative risk (RR) and was estimated as a Mantel-Haenszel estimate (RR_{mh}) by using the histologically normal stomach as a baseline ($RR=1$).¹⁹ The RR_{mh} 's

Table 1 Distribution of the ulcer patients into age groups

Age group (yr)	Men		Women	
	n	(%)	n	(%)
20–39	60	(18.3)	21	(8.6)
40–49	76	(23.2)	40	(16.5)
50–59	93	(28.4)	53	(21.8)
60–69	57	(17.4)	56	(23.0)
70–	42	(12.8)	73	(30.0)
Total	328	(100)	243	(100)

Table 2 Distribution of the non-ulcer controls into age groups

Age group (yr)	Men		Women	
	n	(%)	n	(%)
20–39	145	(32.2)	189	(30.2)
40–49	103	(22.9)	109	(17.5)
50–59	83	(18.4)	124	(19.8)
60–69	64	(14.2)	104	(16.7)
70–	55	(12.2)	98	(15.7)
Total	450	(100)	624	(100)

Table 3 Distribution of ulcer patients by sex and their mean ages in relation to location* of the ulcer

Location of ulcer	Men		Women	
	n	(%)	n	(%)
	Mean age		Mean age	
	yr (SD)		yr (SD)	
Duodenum	145	(44.2)	48	(13)
Pylorus	40	(12.2)	51	(12)
Prepylorus	38	(11.6)	55	(12)
Antrum	12	(3.7)	55	(12)
Angulus	61	(18.6)	58	(12)
Body	32	(9.8)	62	(12)
Total	328	(100)	53	(13)
	243	(100)	59	(14)

*The most proximal ulcer in cases with two or multiple ulcers.

Figure Mean relative risks of duodenal or gastric ulcer in men and women with different grades of chronic gastritis in antrum and body. The risks are adjusted for age and for gastritis on the contralateral site of the stomach (in approximation of the risks of ulcer in antral gastritis, the gastritis in gastric body mucosa is included as a confounding factor, and vice versa). N=normal mucosa, S=superficial gastritis, A1=mild atrophic gastritis, A2–A3=moderate or severe atrophic gastritis.

were adjusted for age by stratification of the cases and controls to age groups as shown in Tables 1 and 2. The calculations of the age adjusted RR_{mh} 's in antrum or body gastritis were further performed with (Figure) and without (Tables 4–6, 8) inclusion of gastritis on the contralateral side of the stomach as a confounding factor. Differences and trends in the estimated risks, as well as the heterogeneity and trends of the risks over the stratified age strata, were calculated and tested as suggested by Breslow and Day.¹⁹ The 95% confidence intervals (CI95) of the relative risks were calculated and are presented as test based limits.¹⁹

Results

The relative risks (RR_{mh}) of coexisting ulcer in the different grades of antral and body gastritis were calculated by (i) inclusion of all cases with duodenal and/or gastric ulcer ('gastroduodenal ulcer'; n=571) into the analysis and, (ii) by separation of subgroups of typical 'duodenal ulcer' (DU, ulcer in duodenal

Table 4 Age adjusted relative risk (RR_{mh}) of duodenal or gastric ulcer in men with different grades of chronic (atrophic) gastritis in antral or body mucosa

	State of antral mucosa				Total
	N	S	A1	A2–A3	
Cases	15	197	63	42	317
Controls	184	196	33	19	432
Total	199	393	96	61	749
RR_{mh}	1.0	11.7	22.2	18.8	
χ^2		97.86	87.12	65.30	
Significance		p<0.001	p<0.001	p<0.001	
CI95		7.2–19.9	11.7–42.2	9.4–37.7	
Test for heterogeneity; χ^2		4.78 (NS)	1.52 (NS)	6.03 (NS)	

Global test of H_0 : $\chi^2=126.8$ (p<0.001).
Test for trend: $\chi^2=102.6$ (p<0.001).

	State of body mucosa				Total
	N	S	A1	A2–A3	
Cases	69	211	15	3	298
Controls	221	155	30	23	429
Total	290	366	45	26	727
RR_{mh}	1.0	3.9	1.1	0.2	
χ^2		63.09	0.002	9.39	
Significance		p<0.001	NS	p<0.01	
CI95		2.8–5.6	0.5–2.1	0.06–0.6	
Test for heterogeneity; χ^2		9.32 (NS)	7.69 (NS)	5.65 (NS)	

Global test of H_0 : $\chi^2=86.41$ (p<0.001).
Test for trend: $\chi^2=1.72$ (NS).

N=normal mucosa; S=superficial gastritis; A1, A2, A3=mild, moderate, or severe atrophic gastritis, respectively.
CI95=95% confidence interval of the RR.

Table 5 Age adjusted relative risk (RR_{mh}) of duodenal and gastric ulcer in men and women with superficial (S) or atrophic body gastritis (A1–A3). Normal body mucosa (N) is the baseline ($RR=1$)

Sex/state of body mucosa	Cases/controls	Relative risk (RR_{mh} ; CI95)	Significance	Heterogeneity/trend between age strata
Duodenal ulcer*				
Men				
N	37/221	1.0		
S	98/155	3.6 (2.4–5.3)	p<0.001	p<0.01/NS
A1–A3	4/53	0.3 (0.1–0.8)	p<0.01	NS/NS
Women				
N	22/289	1.0		
S	42/218	2.1 (1.2–3.5)	p<0.05	NS/NS
A1–A3	2/96	0.3 (0.1–0.8)	p<0.01	NS/P<0.05
Gastric ulcer†				
Men				
N	12/221	1.0		
S	58/155	5.4 (2.9–10.0)	p<0.001	NS/NS
A1–A3	11/53	3.1 (1.3–7.4)	p<0.05	NS/NS
Women				
N	8/289	1.0		
S	45/218	6.2 (3.0–12.7)	p<0.001	NS/NS
A1–A3	23/96	6.1 (2.8–13.4)	p<0.001	NS/NS

CI95=95% confidence interval of the RR.

*Duodenal ulcer cases; †Cases with ulcer in angular area or in gastric body.

Table 6 Age adjusted relative risk (RR_{mh}) of duodenal or gastric ulcer in women with different grades of chronic gastritis in the antrum or body mucosa

	State of antral mucosa				Total
	N	S	A1	A2-A3	
Cases	17	134	58	22	231
Controls	271	246	61	28	606
Total	288	380	119	50	837
RR_{mh}	1.0	7.2	9.9	8.5	
χ^2		65.38	61.01	27.74	
Significance		$p<0.001$	$p<0.001$	$p<0.001$	
C195		4.5-11.5	5.6-17.4	4.1-17.9	
Test for heterogeneity: χ^2		9.73	8.16	11.16	
		($p<0.05$)	(NS)	($p<0.05$)	

Global test of H_0 : $\chi^2=77.44$ ($p<0.001$).
Test for trend: $\chi^2=52.69$ ($p<0.001$).

	State of body mucosa				Total
	N	S	A1	A2-A3	
Cases	57	138	16	7	214
Controls	289	218	47	49	603
Total	342	356	63	56	817
RR_{mh}	1.0	2.7	1.1	0.4	
χ^2		25.61	0.04	3.65	
Significance		$p<0.0001$	NS	NS	
C195		1.8-3.9	0.6-2.2	0.01-1.2	
Test for heterogeneity: χ^2		4.23 (NS)	1.76 (NS)	7.37 (NS)	

Global test of H_0 : $\chi^2=44.21$ ($p<0.001$).
Test for trend: $\chi^2=0.40$ (NS).

N=normal mucosa; S=superficial gastritis; A1, A2, A3=mild, moderate, or severe atrophic gastritis, respectively.
C195=95% confidence interval of the RR.

bulb; $n=211$) and 'gastric ulcer' (GU, ulcer in angular area or in gastric body; $n=186$).

GASTRODUODENAL ULCER

The RR_{mh} of coexisting gastroduodenal ulcer (all cases with ulcer either in duodenum and/or stomach) in the different grades of antral and body gastritis are presented in Tables 4 and 6 and in the Figure. In Tables 4 and 6 the mean risks are adjusted for age alone whereas in the Figure the data are also standardised to take account of coexisting antral gastritis in examining the risks associated with body gastritis, and *vica versa*.

In comparison with the risk of coexisting active ulcer in subjects with normal antral mucosa ($RR=1$), the mean risk of gastroduodenal ulcer was highly significantly above the baseline level ($RR=1$) in subjects who showed antral gastritis (Figure). This risk was increased already in subjects with superficial antral gastritis (grade S; RR_{mh} 9.7 (6.1-15.5) in men and 8.2 (5.7-12.0) in women), and it further linearly

increased in both sexes with an increase in grade of antral gastritis: the RR_{mh} of ulcer reached levels of 25.6 (8.6-76.3) and 14.8 (4.4-49.3), respectively, in men and women who had antral gastritis of grades of A2-A3 (Figure).

The influence of body gastritis on the ulcer risk was opposite to that of antral gastritis. The risk of coexisting ulcer decreased significantly and linearly with an increase in grade of body gastritis (Figure): the mean RR_{mh} 's of ulcer in men with superficial body gastritis (S) or with advanced atrophic body gastritis (A2-A3) were 1.4 (1.2-1.6) and 0.1 (0.04-0.4), respectively. The corresponding risks in women were 1.02 (1.01-1.03) and 0.6 (0.4-0.8) (Figure).

The age adjusted RR_{mh} 's of coexisting active ulcer in subjects with different combinations (phenotypes) of antral and body gastritis, in comparison with risk of ulcer in the presence of a normal stomach (phenotype N/N; $RR=1$), are shown in Table 7. The ulcer risk in both sexes was clearly and significantly increased in most of the phenotypes, although some important differences existed. We emphasise the following three observations (Table 7).

First, the atrophic antral gastritis (A1-A3) that coexisted with non-atrophic body mucosa (N or S) was the phenotype in which the risk of ulcer was highest: the ulcer risk in subjects with phenotype A1-A3/S exceeded 20 for men and 10 for women. Second, irrespective of the grade of gastritis of the antrum, the presence of even mild atrophic gastritis (A1) in gastric body mucosa significantly decreased the risk of coexisting ulcer to levels that were indistinguishable from the baseline ($RR=1$). Third, in comparison with phenotype N/N, the risk of ulcer in all phenotypes of gastritis tended to be higher in men than women.

DUODENAL AND GASTRIC ULCER

The estimates for the age adjusted relative risks, separately for co-existing DU (active ulcer in duodenal bulb) or GU (active angular or high gastric ulcer), in patients with antral or body gastritis are presented in Tables 5 and 8.

The risks of both DU and GU in both sexes were highly significantly higher in the presence of superficial gastritis (S) in the antrum than in the presence of histologically normal antrum (Table 8). There were, however, some differences between DU and GU.

First, with increase in grade of antral gastritis from S to A1-A3 the mean RR_{mh} of coexisting GU greatly increased; this risk exceeded 30 in men and 20 in women if the patient had atrophic gastritis (A1-A3) in the antrum. The risk of coexisting DU did not show such a trend, however (Table 8). Second, with increase in grade of chronic body gastritis from S to

Table 7 Age adjusted relative risk (RR_{mh}) of duodenal or gastric ulcer in men and women with different phenotypes and grades of chronic (atrophic) gastritis. Normal stomach (N/N) is the baseline category ($RR=1$)

Sex/state of mucosa; antrum/body	Cases/controls	Relative risk (RR_{mh} ; (C195))	Significance	Heterogeneity/trend between age strata
Men				
N/N	13/154	1.0		
S/N	37/44	8.4 (4.3–16.2)	$p<0.001$	NS/NS
S/S	135/119	8.5 (7.0–20.0)	$p<0.001$	NS/NS
S/A1	5/15	2.4 (0.7–9.1)	NS	NS/NS
S/A1–A3	11/22	2.1 (0.6–6.8)	NS	NS/NS
A1/N	12/6	25.6 (9.0–72.7)	$p<0.001$	NS/NS
A1/S	42/15	23.2 (10.7–50.0)	$p<0.001$	NS/NS
A1/A1–A3	4/10	3.1 (0.7–14.0)	NS	NS/NS
A2–A3/S	27/9	16.6 (7.1–38.8)	$p<0.001$	NS/NS
A1–A3/N	14/9	15.9 (6.1–41.2)	$p<0.001$	NS/NS
A1–A3/S	69/24	21.0 (10.8–40.9)	$p<0.001$	NS/NS
A1–A3/A1–A3	11/17	6.0 (2.3–15.4)	$p<0.001$	$p<0.05$ /NS
Women				
N/N	14/218	1.0		
S/N	26/55	6.3 (3.3–11.7)	$p<0.001$	NS/NS
S/S	81/159	5.8 (3.3–10.2)	$p<0.001$	NS/NS
S/A1	7/15	4.5 (1.6–12.5)	$p<0.05$	NS/NS
S/A2–A3	4/11	3.2 (1.0–10.1)	NS	NS/NS
A1/S	40/31	11.7 (5.9–23.0)	$p<0.001$	NS/NS
A1/A1	6/14	3.7 (1.1–11.9)	NS	NS/NS
A1/A1–A3	8/22	3.3 (1.2–9.0)	$p<0.05$	$p<0.05$ /NS
A2–A3/S	13/14	7.9 (3.2–19.2)	$p<0.001$	NS/NS
A1–A3/N	6/9	6.5 (2.2–19.0)	$p<0.01$	NS/NS
A1–A3/S	53/45	10.8 (5.7–20.3)	$p<0.001$	NS/NS
A1–A3/A1–A3	12/32	3.3 (1.3–8.7)	$p<0.05$	NS/NS

Normal mucosa; S=superficial gastritis; A1, A2, A3=mild, moderate, or severe atrophic gastritis, respectively.
C195=95% confidence interval of the RR.

Table 8 Age adjusted relative risk (RR_{mh}) of duodenal and gastric ulcer in men and women with superficial (S) or atrophic antral gastritis (A1–A3). Normal body mucosa (N) is the baseline ($RR=1$)

Sex/state of antral mucosa	Cases/controls	Relative risk (RR_{mh} ; (C195))	Significance	Heterogeneity/trend between age strata
Duodenal ulcer*				
Men				
N	5/184	1.0		
S	110/196	16.2 (7.4–35.3)	$p<0.001$	NS/NS
A1–A3	28/52	18.4 (9.3–36.2)	$p<0.001$	NS/NS
Women				
N	6/271	1.0		
S	39/246	5.7 (2.8–11.8)	$p<0.001$	NS/NS
A1–A3	17/89	4.8 (2.1–10.7)	$p<0.001$	NS/NS
Gastric ulcer†				
Men				
N	4/184	1.0		
S	30/196	6.5 (2.5–16.7)	$p<0.001$	NS/NS
A1–A3	55/52	32.2 (15.6–66.5)	$p<0.001$	$p<0.05$ /NS
Women				
N	2/271	1.0		
S	47/246	18.4 (7.2–47.2)	$p<0.001$	NS/NS
A1–A3	41/89	24.4 (10.9–54.6)	$p<0.001$	$p<0.001$ / $p<0.001$

C195=95% confidence interval of the RR.

*Duodenal ulcer cases; †Cases with ulcer in angular area or in gastric body.

A1–A3 the risk of DU decreased significantly in both sexes below the baseline level ($RR=1$), whereas the risk of GU was of same magnitude in both sexes in the presence of S or A1–A3 in the gastric body (Table 5).

Discussion

The present calculations show that a strong association between chronic gastritis and active peptic ulcer exists. In the presence of gastritis, an active ulcer either in duodenum or stomach was several times more common than expected. Although DU and GU do not occur in fundamentally similar circumstances, both seem to show similar features in relation to gastritis. In comparison with subjects with histologically normal gastric mucosa, the risk and probability of coexisting ulcer was markedly and highly significantly increased in the presence of gastritis, this risk and probability being dependent on grade of gastritis in antrum and body. With regard to these risks, however, antral and body gastritis behaved opposite to each other: the risk of active ulcer rose linearly with an increase in grade of gastritis of the antral mucosa but decreased, again linearly, with an increase in grade of gastritis of the gastric body. The calculations showed that the risk of coexisting ulcer was highest in patients who had atrophic gastritis in the antrum and non-atrophic mucosa in the gastric body – that is, gastritis of the B type.³⁰ Active DU or GU appeared over 20 times more common among men with gastritis of this B type than in subjects with histologically normal stomach.

The extremely common occurrence of gastritis in ulcer patients^{1–9,21} and the high risk of coexisting active ulcer in gastritis may suggest that gastritis is causally related to both DU and GU, even though the possibility cannot be excluded that gastritis simply results from the ulcer itself. The present observations on 'dose-response' like relationship between grade of gastritis and general ulcer risk could be, however, considered to support the former possibility. In addition, this is suggested by earlier observations that the healing of ulcer is not accompanied by resolution of the gastritis.^{3,7,22,23} Furthermore, GU typically develops in the stomach at the distal site of the antrofundal junction where the gastritic and atrophic alterations usually are most extensive.^{24–28} These findings may indirectly suggest that gastritis precedes and predisposes to ulcer rather than simply accompanies or follows it.

The negative relationship between active ulcer and body gastritis can be explained by a negative effect of gastritis on capability of the body mucosa to secrete acid and pepsins, and by a consequent decrease in probability of a subject to contract peptic ulcer. Inflammation and atrophy cause a loss of normal acid

and pepsinogen secreting elements in the oxyntic mucosa.²⁸ The acid secretion capacity of the stomach is indeed linearly dependent upon the total mass of parietal cells and upon the number of normal oxyntic glands,^{29,30} and even a mild atrophic gastritis in the gastric body mucosa results in a significant reduction of both basal and stimulated acid secretion.¹¹

The opposite relation of atrophic antral and body gastritis to ulcer risks indicates that antral and body gastritis are independent risk factors. The joint risks, that were directly obtained from the calculation of the risks of co-existing ulcer in different phenotypes of antral and body gastritis were, however, not clear multiplicands of the estimated marginal risks, suggesting that antral and body gastritis nevertheless have some interactions as regards the final ulcer risk. Irrespective of the grade of antral gastritis, body gastritis seems to determine this final risk: the RR_{mh} of coexisting ulcer in patients with even mild body atrophy exceeded only slightly and insignificantly the level of the risk seen in subjects with histologically normal stomach. This strong influence of body atrophy on ulcer risk seems to concern DU in particular.

The present calculations showed that a homogeneity in ulcer risks over the age strata exists. Although the relative frequencies of the DU and GU cases were very dissimilar in young and old age groups of the present series (Table 3), the estimated relative risks of coexisting ulcer did not show, in any of the categories of gastritis, any clear trends or heterogeneity by age (Table 4–8), suggesting that chronic gastritis *per se* is similarly associated with ulcer disease in general. This may further indicate that the DU particularly affects subjects in the early stages of the gastritic progression, whereas GU is more likely to affect subjects in advanced and later phases of this process. This view is supported by the present observations that the risk of coexisting GU, but not of DU, tends to increase with an increase in grade of the antral gastritis, and that the risk of coexisting DU in particular tends to decrease with an increase in grade of the body gastritis. Higher mean and median ages of GU patients compared with those of DU patients may also support this conclusion.

The present study is based on cross section analysis of consecutive routine diagnostic outpatient endoscopies. The biopsy specimens were interpreted by one pathologist but the endoscopies were performed by several endoscopists. This may cause some variability in site of the biopsy specimens from the stomach. This bias, however, probably affects ulcer patients and controls, and possibly is of minor significance. Some more serious biases may, however, emerge from obvious differences in the nature of gastritis in ulcer patients and controls. A limited

number of biopsy specimens may in histology over-emphasise the grade of gastritis in severely patchy lesions as often is the case in gastritis in ulcer patients, in contrast with non-ulcer controls in whom gastritis is more commonly diffuse. An underestimation of the risks may, on the other hand, emerge by inclusion of all ulcer patients into the analysis – for example, ulcer patients with significant NSAID ingestion may increase the proportion of cases with histologically normal stomach among the ulcer patients, thus again decreasing the estimated risks of ulcer in subjects with gastritis.

In spite of the above reservations and threatening biases, the present results may have some practical implications: a coexisting active peptic ulcer disease, either duodenal or gastric, might be improbable and rare if the patient has histologically normal stomach or advanced atrophic gastritis in gastric body. On the other hand, the ulcer disease may be possible if a clear cut antral gastritis is present, and if this gastritis is accompanied by non-atrophic gastric body mucosa.

The cumulative risk of active ulcer may follow these similar guidelines, presuming that gastritis is not a simple result from ulcer itself. Thus, the risk of coexisting ulcer, the short term cumulative risk of active peptic ulcer could be very low in subjects in whom the stomach is histologically normal, but considerable if the subject has chronic antral gastritis. As the mean annual transition risk of a subject to move from normal to a pool of subjects with superficial gastritis, or further from the superficial gastritis pool to a pool of subjects with atrophic gastritis, is between 1 and 2% of the general population,¹⁷ it would be rather improbable that a person would contract gastritis and subsequent DU or GU within the next few years if his/her stomach is now histologically normal.

More positive conclusions on cumulative ulcer risks can be suggested if atrophic gastritis is present in the gastric body. Because the body gastritis is an irreversible lesion,¹⁷ the cumulative, even a late risk of peptic ulcer, and of DU in particular, would be low or even non-existent if a clear cut advanced atrophic gastritis is present in the gastric body.

The above conclusions may suggest that patients can be indeed divided into different categories of ulcer risk on the grounds of absence or presence of different types and grades of gastritis in the stomach as is proposed by Baron³¹ or by Samloff *et al* on the grounds of acid secretion or serum pepsinogen levels.³²

The study was supported from grants from the Yrjö Jahnsson Foundation, Helsinki, Finland.

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