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THE RELATIONSHIP OF CORONARY ATHEROSCLEROSIS AND CHRONIC PEPTIC ULCER: A POSTMORTEM STUDY

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Coronary artery thrombosis and chronic peptic ulceration are among the most common major illnesses encountered in medical practice, and since the incidence of both is known to be increasing, it is tempting to suspect that they may share one or more aetiological factors. Burger (1947) has drawn attention to the striking parallel between the incidence and growing frequency of angina pectoris and peptic ulcer in cases seen in Leipsig between the years 1931 and 1941, and he interpreted this as showing that these diseases have a common cause. If this view were correct, it might be expected that peptic ulcer would be unduly frequent among patients dying from cardiac infarction and, conversely, that in subjects in whom ulcers were found at postmortem examination coronary atherosclerosis would also be excessively common. However, the available evidence on these points is conflicting. A study of postmortem records has led a number of authors, notably Feldman and Morrison (1951) and Morrison and Gonzalez (1952) to conclude that there is a significant relationship between the two diseases, while on the contrary Walsh *et al.* (1941) and Thompson (1954) failed to find evidence of any such correlation. The points at issue are of some practical, as well as academic, importance. An established association between the two diseases would further enhance the need for careful control of anticoagulant therapy in cardiac infarction. Also, if, as some believe, a diet rich in fat predisposes to the development of coronary atherosclerosis, then current views on the dietary treatment of peptic ulcer might require modification.

A relationship between chronic peptic ulcer and coronary atherosclerosis might be held to exist on account of the following considerations:

(1) Both diseases are considered by some to have prolonged and excessive emotional stress as important predisposing causes. While the evidence is by no means convincing, it remains possible that the two conditions have hypothalamic disturbance as a common background. (2) Viscerocardiac reflexes have been studied by several authors (Cullenden & Ivy, 1933: Owen, 1933: Weiss & Ferris, 1934: Jackson &

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Jackson, 1936) and gastrovagal stimulation has been shown capable of producing coronary arterial spasm in human subjects (Morrison & Swalm, 1940). In consequence it has been suggested that chronic peptic ulcer may mediate pathological changes in the coronary arteries via the vagus nerves. Using dogs as experimental animals, Manning *et al.* (1937) were able to demonstrate in the majority of cases that prolonged vagal stimulation would give rise to both coronary thrombosis and peptic ulcers. (3) The concept that dietary factors may be important in the pathogenesis of coronary atherosclerosis has recently attracted much attention. Diets of high fat content have been incriminated and those rich in milk and cream, such as the Sippy variety, have even been considered dangerous to susceptible individuals in middle and later life. Fullerton *et al.* (1953) have demonstrated that alimentary hyperlipaemia following fatty meals is accompanied by an accelerated clotting time in vitro. The dietary hypothesis has received support from Moreton (1947), Morrison *et al.* (1947), and other authors, but Schaffer (1941) and Duguid (1954) do not find the evidence convincing.

The aim of the present study has been threefold :— (*a*) To determine the incidence of chronic peptic ulcer in subjects dying from recent cardiac infarction and/or coronary thrombosis. (*b*) To assess the severity of coronary atherosclerosis in subjects in whom open or healed chronic peptic ulcers were found after death. (*c*) To determine the postmortem incidence of chronic peptic ulcer.

METHODS AND RESULTS.

The postmortem records, numbering 3,421, of the Glasgow Royal Infirmary for the years 1939-1948 inclusive, were examined.

TABLE I.
Distribution of ulcer subjects by age group.

Age (years) Groups	No. of Cases	No. of Ulcers	% age of Ulcers	No. of infarcts.	No. of ulcers	% age of Ulcers
0—10	120	0				
11—24	243	10	4.1	1	0	
25—34	296	30	10.1	1	0	
35—44	496	50	10.8	6	2	
45—54	762	77	10.1	27	2	7.4
55—64	853	85	10.0	49	4	8.2
65—74	544	49	9.0	37	3	8.1
75 +	107	10	9.3	5	0	
TOTAL :	3,421	311	9.1	126	11	8.7

Incidence of peptic ulcers in subjects dying from cardiac infarction. The number of ulcers found in cases dying from cardiac infarction has been compared with the incidence of peptic ulcer in the general autopsy series, and the results are recorded by age group in Table I. At all ages the incidence was less in the infarct-ulcer group, and this was the case whether or not the members of the group were first excluded from the general series. All age groups over 24 years exhibited a remarkably constant autopsy incidence of peptic ulcer; this observation may be correlated with the view held by Doll *et al.* (1951) that at ages in excess of 20 years the expectation of developing a peptic ulcer is also constant.

Coronary atherosclerosis among peptic ulcer subjects. Each case in which an ulcer had been found at autopsy with another in the general series of similar sex and age group and in which at death no evidence had been found of any disease (*e.g.* diabetes mellitus), which might predispose to the occurrence of coronary atherosclerosis. Depending on the degree of atherosclerosis of the coronary vessels found macroscopically at post-mortem examination the cases were separated into three categories :—

(1) Coronary atherosclerosis absent
(2) Coronary atherosclerosis slight
(3) Coronary atherosclerosis moderate or severe

We are aware that information gained from a gross evaluation of the degree of coronary atherosclerosis is necessarily of limited value (Morrison & Johnson, 1950), depending as it must on the impressions of the individual pathologist, but we believe that in the absence of a more reliable standard such evidence as is available should be analysed. The results of such an analysis are presented in Table 2. The groups in which moderate or

TABLE 2.
Distribution of coronary atheroma in ulcer and in control subjects.

Age Groups	Atheroma Absent		Atheroma Slight		Atheroma Moderate or Severe	
	Ulcers	Controls	Ulcers	Controls	Ulcers	Controls
0—14	0	0	0	0	0	0
15—24	10	9	0	1	0	0
25—34	25	21	4	8	0	1
35—44	39	34	8	15	3	1
45—54	36	33	38	40	3	4
55—64	33	27	42	47	10	11
65—74	10	10	25	29	13	10
75 +	1	2	4	4	5	4

State of coronary vessels not recorded in two cases of ulcer.

severe atherosclerosis was found are small, due to the prior removal of cases in which myocardial infarction had occurred. The results in this section could therefore be misleading and instead attention is drawn to the two main groups in which coronary atherosclerosis was either slight or absent. In the latter it will be observed that the ulcer and control series showed little difference in the incidence and severity of atherosclerosis which was, in fact, slightly less frequent in the ulcer group.

Incidence of peptic ulcer. In a total of 3,421 postmortem examinations, active or healed chronic peptic ulcers were found in 311 subjects,: these include 11 in which death was due to myocardial infarction. The gross postmortem incidence is therefore 9.1 per cent. Since chronic peptic ulcer is extremely rare below the age of 10 years, no cases being present in this series, it is sometimes the practice (Ivy *et al.*, 1950) to estimate the incidence above this age. When this is done in the present series the incidence is calculated to be 9.4 per cent. Of the 311 ulcer subjects, 245 were male and 66 were female, and in all 327 chronic ulcers were detected. The latter were gastric in site in 101 cases, duodenal in 219, and anastomotic in 7.

For the purpose of this investigation " peptic ulcer " as found at postmortem is defined as an active chronic ulcer or the visible scar of a healed ulcer. No record has been made of the occurrence of acute gastric erosions. We believe that it is unjustifiable to include them among a series of chronic peptic ulcers because acute erosions may be found associated with a variety of conditions which are not necessarily related causally to peptic ulcers : because acute erosions, if few in number, may be detected only after a long and painstaking inspection of the gastroduodenal mucosa : and because any estimation of the incidence of gastric erosions may be vitiated by the presence of postmortem autolysis.

In order to ensure that death in the cardiac infarction group had been due solely and primarily to acute infarction, only such cases have been included, in company with those in which the cause of death had been specifically stated to be acute thrombotic coronary occlusion. Subjects in whom there was merely evidence of a former healed infarct which had not of itself occasioned death have been excluded. Since postmortem material is necessarily obtained by methods of sampling which would invalidate tests of statistical significance (White, 1953), no such tests have been applied to the recorded figures.

DISCUSSION.

Chronic peptic ulcer in association with coronary atherosclerosis. The available evidence that chronic peptic ulcer is unduly common in patients dying from coronary atherosclerosis does not rest on a firm basis, and is not supported by the results of the present series. Mears (1953), examining the records of 168 consecutive autopsy cases in which death had been due

to acute coronary occlusion, found associated peptic ulcers in 13 subjects ; in 9 of these, however, the ulcers were of the acute variety. Feldman and Morrison (1951) studied the reports of 1,522 consecutive autopsies on subjects who had died at all ages, and noted the presence of peptic ulcer in 6.6 per cent. : 152 cases were found in which death had been due to coronary occlusion and among these the incidence of peptic ulcer was 10.5 per cent. They concluded that there is an excess of peptic ulcers in patients dying of coronary atherosclerosis. Ivy (1947) charted the monthly mortality rates of peptic ulcer and coronary thrombosis over a period of 5 years and, finding that the curves showed general conformity, concluded that there was a definite association between the two diseases. In contrast, Walsh *et al.* (1941) were unable to demonstrate any such association ; on comparing the incidence of peptic ulcer in 576 cases having well-marked coronary atherosclerosis with that in 1,222 subjects who had healthy coronary vessels, they were able to show a difference in incidence of only 0.5 per cent. Thompson (1954), before correction for sex disproportion, found that in a postmortem series comprising 1,000 adults over the age of 10 years the incidence of chronic ulcers and scars was 14.2 per cent. : the incidence of associated peptic ulceration in subjects exhibiting slight atheroma, severe atheroma and frank coronary thrombosis was 18.2, 15.9, and 14.8 per cent. respectively. In the present series peptic ulcer as an associated feature has been found in 8.7 per cent. of patients dying from cardiac infarction, the gross postmortem incidence of peptic ulceration being 9.1 per cent.

Coronary atherosclerosis in association with chronic peptic ulcer. Atherosclerosis is known to be relatively rare in communities existing on diets of very low fat content (Sapper, 1941 : Steiner, 1946), such diets appearing to exert a protective effect. In consequence it has been suggested that diets rich in fat may predispose to the occurrence of atherosclerosis. The evidence has been reviewed by Hueper (1945). Steiner and Domanski (1943), Morrison *et al.* (1948) and Adlersberg *et al.* (1949) stress the importance of hypercholesterolaemia, while Schaffer (1944) and Duguid (1954) consider that the dietary hypothesis of atherosclerosis production still rests on slender foundations. Morrison and Gonzalez (1952) reviewing autopsy records, found evidence of previous cardiac infarction in 27 (23%) of 116 consecutive cases in which death had occurred from one of the complications of chronic peptic ulcer : the incidence of previous infarction among 223 subjects who had died from either an acute or chronic illness other than coronary thrombosis or peptic ulcer was 10.3 per cent. In contrast, Walsh (1941) studied the necropsy records of 2,737 subjects over the age of 20 years : 149 (5%) had chronic peptic ulcers, and the incidence of well-marked coronary atherosclerosis was virtually the same among them as it was in the remaining 2,588 cases. In the present series it has not been possible to show that coronary atherosclerosis is more frequent

among ulcer subjects as compared with control groups of similar age and sex, and this holds true for both gastric and duodenal ulcers, in either sex and at all age levels.

The postmortem incidence of peptic ulcer. In the United States the most recent information on the postmortem incidence of the disease may be obtained from the survey of Mears (1953), who found 4 per cent. of peptic ulcers in a series of 1,000 consecutive autopsies. In that country Held and Goldbloom (1930) believe the postmortem incidence to be about 5 per cent, while Ivy *et al.* (1950), from a study of the American and European literature, consider it to be generally between 5 and 10 per cent. The most important postmortem investigation in Britain has been that of Hurst and Stewart (1929) who found that, in a consecutive series of 4,000 autopsies, 9.55 per cent. showed an active ulcer or the scar of a healed one. The number of consecutive autopsy records in the present series was 3,421, and the ulcer incidence 9.1 per cent. It must be noted, however, that the incidence as estimated recently by different authors shows wide variation, from 1.8 (Gordon & Manning, 1941) to 14.2 per cent. (Thompson, 1954). Such discrepancies arise from varying geographic situation and from the differing natures of hospital populations. For example in the series of Thompson (1954) cases derived from a tuberculosis sanatorium and an infectious diseases hospital were included. A further source of discrepancy in incidence between published series is the grouping together of both acute and chronic peptic ulcers.

SUMMARY.

The postmortem records numbering 3,421 of the Glasgow Royal Infirmary for the years 1939-48 inclusive have been examined. The autopsy incidence of open or healed chronic peptic ulcers was 9.1 per cent. No significant association could be detected between the occurrence of coronary atherosclerosis and peptic ulcer, and vice versa.

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REFERENCES.

Adlersberg, D. Parets, A. D. & Boas, E. P. (1949). *J. Amer. med. Ass.* **141** : 246

Burger, M. (1947) quoted by Card, W. I. in *Modern Trends in Gastroenterology*, Butterworth & Co., London 1952

Cullenden, P. J. & Ivy, A. C. (1933). *Amer. Heart J.* **8** : 507

Doll, R. & Jones, F. A. (1951). *Med. Res. Counc. Spec. Rep. Series No.* 276, H.M.S.O. London

Duguid, J. B. (1954). *Lancet.* **1** : 891

Feldman, M. & Morrison, S. (1951). *Amer. J. dig. Dis.* **18** : 55

Fullerton, H. W., Davie, W. J. A. & Anastasopoulus, G. (1953). *Brit. med. J.* **2** : 250

Gordon, J. S. & Manning, J. J. (1941). *Amer. J. med. Sci.* **202** : 423
Held, I. W. & Goldbloom, A. A. (1930). *Med. Clin. N. Amer.* **14** : 319
Hueper, W. C. (1945). *Arch. Path.* **29** : 117
Hurst, A. F. & Stewart, M. J. (1929). *Gastric and Duodenal* ffilcer. London : Oxford University Press
Ivy, A. C. (1947). *J. Amer. med. Ass.* **132** : 1053
Ivy, A. C., Grossman, M. I. & Bachrach, W. H. (1950). *Peptic Ulcer.* London : Churchill
Jackson, D. E. & Jackson, H. L. (1936). *J. Lab. clin. Med.* **21** : 993
Manning, G. W., Hall, G. E. & Banting, F. G. (1937). *Canad. med. Ass. J.* **37** : 314
Messrs. D. B. (1953). *Surgery.* **34** : 640
Moreton, J. R. (1947). *Science.* **104** : 190
Morrison, L. M. & Swalm, W. A. (1940). *J. Amer. med. Ass.* **114** : 217
Morrison, L. M., Hall, L. & Chancy, A. L. (1948). *Amer. J. med. Sci.* **216** : 32
Morrison, L. M. & Johnson, K. E. (1950). *Amer. Heart J.* **39** : 31
Morrison, L. M. & Gonzalez, W. F. (1953). *Amer. J. med. Sci.* **224** : 314
Owen, S. E. (1933). *Amer. Heart J.* **8** : 496
Schaffer, C. F. (1944). *Ann. int. Med.* **20** : 948
Snapper, I. (1941). *Chinese Lessons to Western Medicine.* New York : Interscience Publishers
Steiner, A. & Domanski, B. (1943). *Arch. int. Med.* **71** : 398
Steiner, P. E. (1946). *Arch. Path.* **42** : 359
Thompson, H. (1954). *Glasg. med. J.* **35** : 326
Walsh, B. J., Bland, E. F., Taquini, A. C. & White, P. D. (1941). *Amer. Heart J.* **21** : 689
Weiss, S. & Ferris, E. B. (1934). *Arch. int. Med.* **54** : 931
White, C. (1953). *Brit. med. J.* **1** : 1284