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MACEWEN MEMORIAL LECTURE, 1953

Ulcer-Cancer of the Stomach

(CARCINOMA EX ULCERE VENTRICULI)

by

MATTHEW J. STEWART
C.B.E., M.D., LL.D., F.R.C.P. (Lond.), F.R.F.P.S.

EMERITUS PROFESSOR OF PATHOLOGY IN
THE UNIVERSITY OF LEEDS

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Sir William Macewen as Surgeon Rear-Admiral, 1914–18

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ULCER-CANCER OF THE STOMACH
(*CARCINOMA EX ULCERE VENTRICULI*)

The invitation to give the seventh Macewen Memorial Lecture reached me as I was on the point of departure for a year's visit to Australia and New Zealand, and in consequence its delivery has been long delayed. That I should be so honoured by my Alma Mater had never crossed my mind, and when I thought of the distinguished group of previous Macewen Lecturers, of Harvey Cushing and Ballance, René Leriche and Sauerbruch, Grey Turner and Geoffrey Jefferson, I felt profoundly conscious of my inadequacy for the task. My predecessors, all of them distinguished surgeons, have paid glowing tribute, in a way which I cannot hope to emulate, to our great Macewen and his epoch-making contributions to surgical knowledge and practice, but in one important respect I have an advantage over them all. I was his student. More than this, I was a " Macewenite ", and those of you who were students of this school in the early years of the century know what this implies. We were not only his students: we were also his devoted and whole-hearted admirers. He was a king who could do no wrong!

Macewen was a born teacher. Individualist he surely was, and in his teaching he spoke essentially from his own individual and rich experience. He certainly quoted authority, sometimes with approval,

often with keenly critical comment. At that time it was his custom, in the systematic lecture course, to devote the first term of the winter session to general pathology, with particular emphasis on inflammation and necrosis. For the second term's lectures, the class was invited to select some special branch of surgery. In my year we chose the most obvious and, I imagine, the most generally popular—the surgery of the central nervous system. Macewen was a delightful lecturer—lucid, forceful, convincing, inspiring—his discourse enlivened with witty and often sarcastic and critical comment on such current teaching as he found unacceptable. I cannot recall that he ever recommended a text-book of surgery. Indeed, I think he advised against the whole brood, and I well remember his description of how, in his view, text-books—and especially surgical text-books —are usually written. You purchase or otherwise acquire all the latest editions of the most popular existing manuals and retire with them to your study —or to the drawing-room for that matter. There you get busy with scissors, paste and a scrapbook, picking and choosing from this text and that, and in due course a new text-book emerges!

Macewen's clinic was a popular one, and as there was apparently no limit to the number who might enrol, teaching conditions were far from ideal. His triumph over such adverse physical factors was complete, and absenteeism was minimal. The Socratic method was much employed, and there were usually one or two members of the class who were willing to essay an answer, however difficult or awkward the

question. One such I vividly recall, Charles Samson Thomson, from Ayr Academy, who later became medical officer of health for the City of Belfast. No answer or only an unacceptable answer to a question by Macewen being forthcoming, " And what does the gentleman from Ayr Academy have to say about this? " Sir William would ask. Charlie never failed with an immediate, pertinent and usually witty response, to the great delight of the class.

Macewen, in those days at least, was one of the staunch supporters of chloroform anaesthesia. He held that if properly administered it was an eminently " safe " anaesthetic. It was his custom to give half-a-dozen clinical lectures on anaesthesia at the beginning of the winter session and to hold a small written examination afterwards. Only those who passed this test were allowed to administer chloroform, even under supervision. In those early years of the century, the methods of inducing anaesthesia were simple but effective, and if Sir William's principles and precepts were faithfully adhered to, chloroform anaesthesia certainly appeared to be perfectly " safe ". The whole procedure was based on the physiological reactions of the patient, to which the closest attention was paid both before and throughout the operation. Measured dosage was still in its infancy and with its advent there came also the risk of a false sense of security. I am sure, however, that Macewen would never for a moment have allowed any relaxation of his own very strict rules for the control of anaesthesia by observation of the patient's reactions.

With these few reminiscent remarks I must

now proceed to the subject of my lecture, the pathology of ulcer-cancer or *carcinoma ex ulcere* of the stomach.

The observations which follow are based on a 29 years' study of partial, occasionally total, gastrectomy specimens submitted for pathological investigation by my surgical colleagues in Leeds, to whom I am deeply indebted for permission to make use of their material. Whenever possible the specimen was despatched from the operating theatre soon after its removal and before it had been placed in fixative. As far as possible each was examined and described at once, after being laid open along the line of the greater curvature unless there was some contra-indication to this procedure. It was then pinned out flat on a formalin-soaked lint-covered board, mucosal surface uppermost, and placed in a tank of 10 per cent formol-saline for 24 hours or longer. A sketch drawing was made of each specimen containing a lesion, either in the fresh state or after fixation. Blocks for histological examination were taken after two or three days' fixation, usually several from each specimen, the site of each block being marked in red ink on the sketch. In selected instances paraffin sections were mounted directly on lantern plates in addition to the usual microscopic slides. This often allowed the whole width of even a large ulcer or of a tumour up to 3 inches in diameter to be reconstructed. In all, 1503 surgical specimens of gastric ulcer or gastric cancer were investigated in this way, covering the years 1921 to 1949 inclusive (Table I).

TABLE I

LIST OF CASES INVESTIGATED

	1921–40 (*20 yrs.*)	*1941–49* (*9 yrs.*)	*1921–49* (*29 yrs.*)
Chronic gastric ulcer (independent)	459	476	935
Carcinoma (independent)	230*	248†	478‡
Ulcer-cancer	51	52	103
	740	776	1516
Independent ulcer and cancer co-existing in the same stomach	7	6	13
Total cases	733	770	1503

* Including 4 cancers of the cardia.

† Including 64 cancers of the cardia.

‡ Including 68 cancers of the cardia.

POSITION OF THE LESION

It is most unusual for a chronic peptic ulcer of the stomach to occur elsewhere than in more or less close relation to the lesser curvature, and, in rather less than one-third of those so situated, the caudal margin of the ulcer comes within 3 cm. of the pylorus. Simple chronic *gastric* ulcers arising at the cardia or in relation to the greater curvature are exceedingly rare. Carcinoma, on the other hand, is not only more widely distributed; it arises in nearly two-thirds of cases in the pyloric canal and in about one-sixth in the region of the cardia. These figures are based on post-mortem room findings. Operation specimens, until recent years, have been highly selective, and the incidence of ulcer-cancer as

observed in routine surgical material—in respect, that is to say, of the frequency with which gastric carcinoma shows evidence of antecedent simple ulceration—has been considerably affected in the last 12 years or so by the activities of the thoracic surgeon. In my earlier series of cases, prior to 1941 (Stewart, 1947) there were in all only 4 instances out of a total of 230 cases of carcinoma of the stomach where the tumour had originated at the cardia and had been treated by either total or upper partial gastrectomy. In the succeeding 9 years (1941–9 inclusive) 64 such specimens out of a total of 248 gastric cancers were received.

Now since chronic peptic ulcer of gastric origin is extremely rare in the region of the cardia, it might be argued that cases of gastric carcinoma arising in this situation should not be taken into account in assessing the frequency with which, in surgical material, malignancy has arisen in a pre-existing simple chronic peptic ulcer. It was decided, however, that cases of cardiac cancer of gastric origin should continue to be included, while realising that this would have the effect of slightly lowering, as compared with the earlier series, the proportion of carcinomas which might be regarded as originating *ex ulcere*. Obviously this difficulty does not arise in assessing the frequency with which the simple chronic ulcers in the series had undergone malignant change.

Of the 52 cases of ulcer-cancer so diagnosed in the 9-year period 1941–9, the lesion was situated in the pyloric canal in 24 instances (Table II), in the

rest of the lesser curvature region in 28. That is to say, in 24 cases the lower (caudal) margin of the ulcer lay within 3 cm. of the pyloro-duodenal junction, in 28 cases the lower margin of the lesion was 3 cm. or more from the pylorus.

TABLE II

INCIDENCE OF ULCER-CANCER IN (*A*) THE PYLORIC CANAL AND (*B*) THE REST OF THE LESSER-CURVATURE REGION IN THE 9 YEARS' PERIOD 1941–49 (GASTRECTOMY SERIES)

	Ulcer	*Ulcer-cancer*	*Percentage of simple chronic ulcers becoming malignant*
Pyloric canal	149	24	16·2
Rest of lesser curvature	379	28	7·4
Total	528	52	9·8

	Cancer	*Ulcer-cancer*	*Percentage of carcinomas originating in simple chronic ulcers*
Pyloric canal	165	24	14·5
Rest of lesser curvature	70	28	40·0
Total	235	52	22·0

It has been argued that if antecedent chronic ulcer were an important factor in the aetiology of gastric carcinoma, there should be a much higher incidence of malignancy in the lesser curvature region as compared with the pyloric than is shown in published figures. Whatever the relationship of

ulcer and cancer, it is an indisputable fact that cratered lesions in the pyloric region are much more likely to be malignant than similar lesions higher up on the lesser curvature and should be treated accordingly. It may well be, however, that some additional factor such as greater mechanical trauma is responsible for a higher incidence of cancer in simple ulcers of the pyloric canal.

Criteria for the Pathological Diagnosis of Ulcer-Cancer

I am here concerned chiefly with the anatomical and histological criteria for the diagnosis of *carcinoma ex ulcere*, but in assessing the value of these criteria, the clinical aspects of the cases studied have also been brought into consideration. It must be admitted at the outset that in many cases the difficulty of making a diagnosis on purely anatomical grounds is still very great and in some cases insuperable. If, however, clinical facts are also taken into account the number of doubtful cases is appreciably reduced.

We are dealing, of course, with chronic ulcers only, and usually with those of long standing. Such ulcers have led almost invariably to complete destruction of the whole thickness of the muscular coat over an area corresponding more or less closely with that of the ulcer crater. If healing has proceeded to any extent, however, and this is frequently the case in surgical material, the gap in the muscularis may be considerably greater than that in the mucosa and submucosa. In the active stage of a chronic ulcer

the muscular coat either terminates abruptly in the lateral walls of the crater or turns upwards into the ulcer floor, this latter phenomenon depending on the contraction of the fibrous tissue in the deeper and more central parts of the lesion, including the serosa and subserosa. Invariably, in the active phase, the submucosa is widened by oedema, inflammatory-cell infiltration and cellular fibrosis, leading especially to great widening of the interval between the muscular coat and the muscularis mucosae. If the ulcer enters upon an indolent, non-progressive but also non-healing phase, these appearances may last for a long time—months, possibly years. After healing has set in, the ulcer crater gradually loses its zone of fibrinoid necrosis and the purulent exudate which clothes the surface and becomes much shallower, while the margins flatten out and cease to be undermined.

Two other important changes take place at this time. The epithelium starts to grow in from the margin and the severed ends of the muscular coat and muscularis mucosae gradually approximate and ultimately blend with each other. To the importance of this phenomenon of marginal muscular fusion in relation to the histological diagnosis of ulcer-cancer both Turnbull (unpublished lectures; quoted by Newcomb, 1932–3) and Newcomb have drawn special attention (Newcomb, 1930, 1932–3). It is very exceptional for a like phenomenon to occur in secondarily ulcerated primary carcinoma.

Dible (1924–5) has stressed the importance and frequency of local chronic vascular changes, especi-

ally obliterative endarteritis, as an accompaniment of chronic peptic ulcer. He had several cases, however, in which these changes were present in association with primary cancer. Newcomb (1932–3) found endarteritis or thrombophlebitis in 72 per cent of his 161 cases of chronic gastric ulcer, but as he also found these conditions present in 16 per cent of carcinomas of the *colon* (Newcomb, 1930) he considers them to be of little value as a diagnostic point in ulcer-cancer of the stomach. It is certain, however, that endarteritis obliterans and organising or organised thrombo-angiitis are far more frequent and striking in simple chronic ulcer (and ulcer-cancer) than in primary carcinoma. In my opinion they should at least be regarded as providing corroborative evidence when found in association with the other histological criteria of ulcer-cancer mentioned above.

In order, then, to establish a pathological diagnosis of ulcer-cancer it is necessary in the first place to show the intimate topographical relationship of the two lesions—unmistakable carcinoma and simple chronic ulcer. The most straightforward case is where there is a small focus of invasive carcinoma in the margin of an otherwise benign peptic ulcer of obvious chronicity, a type of case with which the pathologist is by no means unfamiliar. More often the malignancy has progressed beyond this stage and the difficulty is to establish the fact that a simple ulcer had preceded it. Occasionally, tumour tissue is present around most of the margin, in rare instances all round it, while the centre of the lesion