

*Leading article*

## Cancer after peptic ulcer surgery

Almost 30 years have elapsed since Krause<sup>1</sup> showed that patients tended to die prematurely in the years after surgical treatment of peptic ulceration by Billroth II partial gastrectomy. Tuberculosis, carcinoma of the stomach remnant, suicide and alcoholism headed the list of causes of death. The intervening years have seen a dramatic fall in the incidence and relative importance of tuberculosis but the role of ulcer surgery in the development of gastric and other forms of cancer continues to excite controversy. This debate is fuelled by the publication in this issue of *Gut* of the latest paper<sup>2</sup> detailing outcome in ulcer patients operated on in the St James Hospital, Balham, by Mr Norman Tanner and his colleagues. The Balham patients form a large and important study group; all underwent surgery at least 25 years ago, only 11% have been lost to follow up, and death certificates have been reviewed from the 2768 patients who have died to date. As might be expected, most patients were treated by some form of gastric resection.

Once 20 years had elapsed, these patients exhibited a significant excess risk of dying not only from cancer of the stomach (4.5 fold increase) but from cancer of the biliary tree, pancreas, breast, bronchus, bladder, oesophagus and large bowel. Indeed after 20 years, the risk of dying from any form of cancer rose three fold after ulcer surgery while that of dying from non-neoplastic disease increased 1.6 fold. Interestingly, before this time interval previous ulcer surgery did not increase the risk of cancer death and actually decreased the chances of succumbing to non-neoplastic disease.

This paper adds new impetus to the debate about the long term outcome after ulcer surgery. Is the observed increase in cancer mortality real? Is it important when viewed in the context of all causes of death in these patients? Can we and should we alter clinical practice in an attempt to avoid or negate the problem?

While it is by no means universally agreed, a growing number of publications support the contention that previous surgery for peptic ulcer does increase the risk of dying from gastric cancer. As the Balham study shows, the risk seems greatest for patients with gastric ulcer and their risk may be realised earlier than in patients with duodenal ulcer. If diminished acid secretion is important in the formation of carcinogens, it can be argued that gastric ulcer patients may already have been at risk before surgery was carried out. The risk of dying from gastric cancer may be greater after Billroth II than Billroth I gastrectomy,<sup>3</sup> opening the possibility that other factors such as bile reflux could be implicated in carcinogenesis. It must be emphasised that not all studies report an increased risk of death from gastric cancer. For example, the important Edinburgh study<sup>4</sup> showed no increase in 779 patients, 86% of whom were treated by partial gastrectomy. As the authors point out, however, the average interval between gastrectomy and death was 18.9 years in these patients, and it is conceivable that an excess

mortality from gastric cancer may still emerge as the length of follow up increases. While fewer data are available to allow evaluation of risk after truncal vagotomy and drainage, there is growing evidence, at least in the case of duodenal ulcer patients, that cancer risk is still increased. While the Balham study shows no increase until 20 years after duodenal ulcer surgery, Watt and his colleagues<sup>5</sup> report a three fold increase in death from gastric cancer in such patients followed for a minimum of 15 years. Any theoretical advantage in this context of continuing acid secretion after vagotomy has to be set against the potential hazard of retaining a cancer-prone distal stomach if such surgery does indeed influence the process of carcinogenesis.

In the Balham study,<sup>2</sup> the incidence of death because of cancer of the stomach, biliary tract, pancreas and lung was as expected in the first 15 to 20 years, but a large and significant excess mortality was found thereafter. On the other hand, other forms of cancer and non-neoplastic disease caused no overall excess mortality in that later excesses were offset by an actual decrease in risk during the early years. This apparent early benefit is difficult to explain and must be set against the observation in Edinburgh that the survival curve for ulcer patients begins to diverge from that of the general population from the time of operation, that the decline is apparent in all age groups, and that the mean adverse shift of the survival curve for the various age groups is some nine years.<sup>4</sup>

With regard to the risk of dying from some other form of cancer, lung cancer looms large as a much greater menace than cancer of the stomach or other organs. In the Balham study no less than 323 patients died from lung cancer after 20 years, as opposed to only 37 deaths from gastric cancer, a difference mirrored in other studies.<sup>4,5</sup> Given that over 80% of ulcer patients are habitual smokers at the time of operation and that few cease smoking thereafter,<sup>4</sup> this is hardly surprising. It is also difficult to believe that smoking does not play some role in the development of other cancers, notably those arising in the pancreas and large bowel. As Caygill *et al*<sup>2</sup> point out, however, the common latency period of some 20 years in their study leaves open the possibility that gastric surgery *per se* may have some initiating role in the process of carcinogenesis. While other studies support an association between ulcer surgery and cancer of the lung, pancreas and large bowel,<sup>4,5</sup> it must be stressed that the link to other forms of cancer is more tenuous and as in the Balham study,<sup>2</sup> is often based on very small patient numbers.

How important are these observations? My own interpretation is that the link between previous ulcer surgery and gastric cancer is real and that the risk increases with the passage of time.<sup>6</sup> The data are strongest in the case of gastric resection but we have no room for complacency with regard to truncal vagotomy and drainage. It will be of immense interest to determine whether with the passage of time, any association emerges between gastric cancer and highly selective vagotomy. To my mind, further data are needed to determine whether ulcer surgery does indeed influence the risk of developing cancer at sites other than the stomach. We have a long way to go before disproving the hypothesis that such cancers, and for that matter some gastric cancers, are a result of factors in the patient's life style and of the potential factors, cigarette smoking must remain the prime suspect. It is certain that we must not over react to the debate and that the problem must be kept in perspective. Non-neoplastic disease and lung cancer between

them killed 991 patients 20 years or more after ulcer surgery in Balham, whereas gastric cancer killed only 37.<sup>2</sup> In Edinburgh,<sup>4</sup> ischaemic heart disease, lung cancer, cerebrovascular accidents, chronic bronchitis and emphysema, and bronchopneumonia caused 267 deaths as opposed to 16 due to large bowel cancer, 11 to pancreatic cancer and eight to gastric cancer. While in theory, endoscopic screening could detect gastric cancer after ulcer surgery and allow its prompt treatment, thoughtful studies<sup>7,8</sup> of the problem doubt its justification in any ageing population with a high incidence of cardiopulmonary disease who will be far from ideal candidates for more extensive gastric surgery. In the Edinburgh study,<sup>4</sup> the excess mortality from smoking related disease was more than three times greater than the total mortality from gastric cancer. One is forced to agree with Logan and Langman<sup>7</sup> that greater efforts to persuade patients to stop smoking would be of greater benefit than any endoscopic screening programme. We must continue to accrue evaluable data, we must continue to test hypotheses regarding an association between ulcer surgery and cancer but we must not be stampeded into an ill judged flight from an exceedingly useful method of treating peptic ulcer that has stood up well to the test of time.

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#### References

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