Introduction to the Clinical Papers

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Reflux oesophagitis and peptic ulcer are both considered to be acid-related diseases: gastric acid is not the cause but plays an important role in their pathogenesis. Eighty years ago, Schwarz stated that without acid, there is no ulcer and this law remains true today (Schwarz. Brun's Beitr Klin Chirurgie 1910;67;96-128). This emphasizes that the best treatment for peptic ulceration is still inhibition of gastric acid secretion.

The most efficient way to control gastric acid secretion is to inhibit the acid pump of the parietal cell in the oxyntic mucosa; omeprazole achieves this rapidly and efficiently without side effects in the clinical setting. Accordingly, there is increasing evidence for the superiority of omeprazole over all other antiulcer drugs and for its safety in short-term use.

Fears have recently been expressed over the risk of inducing complete, or near complete, achlorhydria which is an advantage for the acute healing of ulcers but which is not apparently required for the long-term maintenance treatment of peptic disorders (i.e. to prevent recurrences). Options such as reducing the dose of the acid inhibitor or using intermittent therapy should be considered.

It is important to remember that the clinical situation in humans is very different to that found in the animal models discussed in the non-clinical papers. This was exemplified by a consideration of the gastrin response to acid inhibiting therapy. Before surgery, in patients with duodenal ulcer, serum gastrin levels range between 20 and 50 pmol/l if measured hourly for 24 h. After vagotomy, these

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levels are 2 or 3 times higher. Treatment with omeprazole, 20 mg daily, produces gastrin levels similar to those seen after vagotomy. In pernicious anaemia, in which there is atrophy of the oxyntic mucosa leading to the loss of gastric acid secretion, there is hypergastrinaemia with much higher gastrin concentrations than those seen after vagotomy [in excess of 1,000 pg/ml (500 pmol/l)]. Despite these extreme conditions, gastric enterochromaffin-like (ECL) cell carcinoids have been observed in only a few patients with pernicious anaemia and only after this disease has been present for more than 10 years. Furthermore, these patients had severe atrophic gastritis with intestinalization of the oxyntic mucosa. Gastric ECL cell carcinoids have been found in patients with hypergastrinaemia due to the Zollinger-Ellison syndrome only if the gastrinoma was part of the MEN-1 syndrome. During maintenance treatment with omeprazole, 20 mg daily, the basal serum gastrin concentration is only 50-120 pg/ml. These findings suggest that treatment with omeprazole does not represent a significant risk for the development of gastric ECL cell carcinoids in man.

The clinical papers which follow in this section provide further evidence for the clinical efficacy and long-term safety of omeprazole.