Pertechnetate and the Stomach—A Continuing Controversy

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Technetium-99m is concentrated by the stomach following intravenous injection. This principle allows the detection of ectopic gastric mucosa and has been used to develop a noninvasive test of gastric secretion. The cellular site of concentration is controversial, however, with evidence implicating both the acid-secreting parietal cells, and the mucus secreting epithelial cells of the gastric mucosa. This evidence is reviewed and appraised. It is suggested that the primary mechanism lies in the mucous cell but that total gastric activity following pertechnetate reflects the health, surface area, and blood flow of the mucous epithelium.

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Recent articles by Sfakianakis and co-workers (*1*,*2*) have highlighted the value and extensive clinical use of abdominal imaging with pertechnetate in the diagnosis of ectopic gastric mucosa, particularly in a Meckel's diverticulum. In spite of this wide experience and evaluation, however, there remains controversy as to the cellular site of uptake of pertechnetate in the stomach. The argument lies between the parietal cell, which is confined to the gastric pits that line the body and fundus of the stomach, and the mucus secreting epithelial cells that line the whole of the mucosa of the stomach. Sfakianakis and colleagues have briefly summarized the evidence that the mucus secreting surface cells of the gastric mucosa are responsible (*1*), but there remains a good deal of evidence that the parietal cell is also significantly involved. This evidence is highlighted by the work of Taylor and his colleagues (*3*), who have developed a noninvasive pentagastrin test to measure gastric uptake of pertechnetate (Tc-99m) by external counting, a test that correlates well with acid output as measured by the conventional pentagastrin test. The time seems ripe for a reappraisal of the evidence available in this controversy.

EVIDENCE FOR PARIETAL SECRETION

Technetium is a member of Group 7A of the periodic table and it is reasonable to assume that gastric concentration of pertechnetate might be similar to that of chloride (since chlorine is a member of Group 7B) through the formation of pertechnic rather than hydrochloric acid by the parietal cell (*4*). This assumption is supported by the various studies that have shown a correlation between acid output and pertechnetate clearance (*5–7*) and the demonstration of good separation between duodenal and gastric ulcer patients, both on clearance (*6*) and on gastric uptake (*3*), when the stomach is maximally stimulated by pentagastrin. In the study of Wine and colleagues (*7*), denervated gastric pouches (Heidenhain and antral) were fashioned in dogs, and Tc-99m output was measured with histamine stimulation. They found technetium output of a Heidenhain pouch to be related to acid output and to volume in a dose-related manner, but the antral pouch was unaffected by histamine. Various workers have used technetium clearance as a measure of gastric blood flow. Bickel et al. (*5*) showed in man that for a given level of stimulation with an histamine agent, good proportionality existed between gastric acid secretion and gastric clearance of pertechnetate (infused to maintain a constant blood level), aminopyrine, and iodide. The relationship changed at different levels of stimulation, but their calculations were based on the assumption that pertechnetate secretion is predominantly parietal but with a nonparietal contribution passively related to blood level. Irvine and colleagues (*8*) found that the clearance of pertechnetate correlated closely with the volume of gastric secretion, and to a lesser extent with acid and intrinsic-factor output, using histamine stimulation in

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patients with pernicious anemia, peptic ulcer, and normal stomachs. Meredith and Khan (*9*) measured gastric blood flow using an electromagnetic flowmeter in dogs with surgically prepared stomachs having a single venous drainage. Their preparation measures total rather than mucosal gastric blood flow, and they found a correlation between technetium clearance and blood flow in the basal state; there was, however, great variability from animal to animal, and the results were unaffected by histamine infusion. Taylor et al. (*6*) showed that pertechnetate clearance correlates well with clearance of aminopyrine (C-14) and tritiated quinine in rats when measured under basal conditions. In man they measured technetium clearance and acid secretion simultaneously, under basal conditions and with stimulation by pentagastrin. They found that in all cases where there was a rise in acid secretion there was a rise in pertechnetate clearance, the increased clearance tending to precede the rise in acid secretion.

The studies of Taylor and co-workers (*3*) showed that external counting of gastric pertechnetate activity correlates well with acid output in normal people and patients with peptic ulcer; they also found a distribution of uptake between normals and patients with duodenal ulcer comparable to that found with the conventional pentagastrin test. More recently Keane and co-workers (*10*) have confirmed a good separation between duodenal-ulcer patients and normals when rate of technetium uptake by the stomach following pentagastrin is measured, but these workers have been unable to confirm any correlation with acid output as measured by the conventional pentagastrin test.

The effect of cimetidine (a potent inhibitor of acid secretion) on gastric mucosal uptake is controversial, being reported variously either to inhibit pentagastrin-stimulated uptake in man (*10*) but to have no effect on basal secretion in man (*11*), or to enhance it in dogs (*12*) and possibly man (*13*).

A single autoradiographic study from Germany in 1967 has demonstrated concentration of Tc-99m in the parietal cells in cats and man (*14*). Both pertechnetate and iodine-131 were studied, and it was concluded that technetium is selectively secreted by the parietal cells, whereas by contrast iodine is secreted by the chief and mucosal cells. Antral mucosal activity was dismissed as due to contamination with fundal secretion, but graphically there was as much activity in the antrum as in the fundus with both radionuclides.

EVIDENCE FOR NONPARIETAL SECRETION

Many animal studies have shown that antral tissue, although devoid of parietal cells, concentrates pertechnetate (*15–17*). In man this evidence is supported by the ability to visualize gastric mucosa in the absence of parietal cells: in pernicious anemia (*18,19*), in the retained gastric-antrum syndrome (*17,20*), and in Barrett's esophagus (*21*).

A large number of autoradiographic studies have been performed with pertechnetate in animals. Activity has been shown in the columnar mucous epithelium of the stomach in rats (*18,22*), dogs (*18,23,24*), and mice and cats (*18*), with no activity in the parietal or chief cells. It has also been shown that regenerating gastric mucosa in the dog concentrates pertechnetate avidly in the almost complete absence of parietal cells (*25*).

In man it has been shown that an increased gastric uptake of pertechnetate occurs in patients with gastric ulcer following treatment with carbenoxolone (*11*). This drug restores normal epithelial-cell function and mucus secretion in such patients (*26*). In pernicious anemia, time-activity curves following intravenous pertechnetate show similar uptake in the fundus and antrum, whereas in normal stomachs fundal uptake is markedly greater than antral uptake (*27*).

DISCUSSION

The evidence, therefore, shows that pertechnetate is concentrated with avidity by the whole stomach in the presence or absence of parietal cells, yet with a correlation with acid output when this is present. At a cellular level this uptake must either (a) occur in the mucus secreting epithelium, or (b) two different cell types must be responsible—the mucous epithelial cell and the parietal cell. There is autoradiographic evidence for both of these, although the only study performed in man showing uptake in the parietal cell (*14*) has not yet been repeated and confirmed. If the mucous epithelial cell is primarily or even solely responsible, pertechnetate would be secreted as a nonparietal component of gastric secretion. The established correlation with acid secretion would then be explicable as a reflection of blood flow rather than parietal cell activity.

Pentagastrin increases gastric mucosal blood flow (*28*) as well as the volume and acidity of gastric secretion, with the peak in volume preceding that of acid (*29*). The studies of Taylor et al. (*6*), measuring acid output and technetium clearance in response to pentagastrin, showed remarkably similar responses, with technetium clearance peaking before acid output.

Cimetidine decreases pentagastrin-stimulated blood flow (*28*), which is compatible with the inhibition of pentagastrin-stimulated pertechnetate secretion shown by Keane and colleagues (*10*). The enhancement of mucosal accumulation of pertechnetate by cimetidine without pentagastrin stimulation (*12,13*) is more difficult to explain. Cimetidine has no effect on basal gastric mucosal blood flow (*28*) in spite of profound inhibition of acid secretion, whereas under pentagastrin stimulation cimetidine administration results in parallel decreases of acid output and blood flow (*30*). Under basal condi-

tions cimetidine administration will therefore decrease the acidity of the gastric contents without altering mucosal blood flow. If intragastric acidity enhances the transfer of pertechnetate from cell to lumen (perhaps by promoting stable complex formation in the lumen and preventing back diffusion into the mucosa), this might explain the accumulation in cells rather than lumen when acid secretion is inhibited by cimetidine. Comparison with perrhenate is relevant here. Perrhenate (Re-188) is more difficult to reduce than pertechnetate ion and, although concentrated in the gastric mucosa, is not lost into the gastric lumen in any great quantity (*31*).

In pernicious anemia gastric secretion of pertechnetate is seen throughout the stomach, but uptake values are less than in the normal subject or one with duodenal ulcer (*3*). In this condition the gastric contents are also neutral but the health of the mucosa is impaired with rapid turnover and loss of mucosal cells (*32*) and impairment of mucus secretion. A similar gastritis is seen in gastric-ulcer patients, in whom the restoration of normal mucous-cell function by carbenoxolone (*11*) will increase pertechnetate uptake.

It is likely that the surface area of the stomach also influences pertechnetate uptake. In pernicious anemia, where there is a loss of the normal rugal folds in the body and fundus, uptake by the stomach is reduced but is uniform overall (*27*). Back-diffusion of pertechnetate into the gastric mucosa should also be considered, since absorption of pertechnetate from the stomach by simple diffusion in the presence of a concentration gradient has been claimed (*4*). Further work is required to establish whether this varies with the health of the gastric mucosal barrier.

It seems possible, therefore, that pertechnetate is concentrated specifically by the mucous epithelial cells of the stomach but that the scale of this concentration is influenced by the surface area, blood flow, and the health of the mucous epithelium. It is also possible that the pH of the gastric contents will influence the degree of secretion or mucosal retention of pertechnetate. None of the evidence previously interpreted as suggesting that parietal cell secretion of pertechnetate occurs is incompatible with such a concept, with the exception of the autoradiographic evidence of Meier-Ruge and Fridrich (*14*). Further such studies in man are clearly necessary. Even this study is not incompatible with a two-component hypothesis for the secretion of pertechnetate, where most of the ion is handled by a specific nonparietal mechanism with a small nonspecific mechanism shared with chloride through the parietal cell. This would be similar to the handling of iodide by the stomach. Howell and van Middlesworth (*33*) measured gastric iodide and chloride clearance in dogs with and without histamine stimulation and perchlorate inhibition; they concluded that there could be two mechanisms for the gastric secretion of iodide: a specific system responsible for up to 90% of the total iodide clearance, which could be 95% suppressed by perchlorate, and a nonspecific mechanism, shared with chloride but unaffected by perchlorate, responsible for the remainder.

The clinical implications for the detection of ectopic (*2,34*) and particularly nonparietal (*20*) gastric mucosa have already been well documented. The noninvasive pentagastrin test developed by Taylor and his colleagues (*3*) is not necessarily invalidated if parietal secretion per se is not being measured, since the correlation with blood flow, in spite of this, provides a useful noninvasive measure of acid secretion, except in patients who have atrophic gastritis, where the impairment of acid secretion is significantly greater than the impairment of mucous-cell function.

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