Gastric Secretion of Iodide at Low Serum Iodide Levels. (17722)

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Several reports in the literature show that the concentration of iodide in gastric juice may exceed concurrent plasma iodide levels many fold(1,2,3,4). Davenport(5), in an attempt to elucidate the mechanism of this phenomenon, found an inverse curvilinear relationship between the concentration of iodide in gastric juice and the plasma iodide level, when the latter was in the range of 0.1 to 3.0 millimol per liter. No correlation between the concentration of iodide in the gastric juice and other variables of gastric secretion was observed. Since pouch dogs were used in these studies and gastric secretion was stimulated with histamine, one must presume that the secretion studied was consistently in the acid pH range.

The experiments reported here extend the observations of Davenport to the gastric excretion of iodide at consistently low serum iodide levels, and to its secretion in alkaline gastric juice. It was hoped that under these conditions a correlation between the gastric excretion of iodide and other variables of gastric secretion would become apparent. These expectations were, at least in part, fulfilled. A study of the iodide concentration in alkaline gastric juice was made possible by the use of a preparation recently described by Morton and Stavraky(6). The use of radioactive iodine as a tracer made it feasible to study the gastric excretion of iodide at low serum iodide levels; by means of the isotope the injected iodide could be distinguished readily and in small amounts from the iodine normally present in the body.

Methods. The gastric excretion of radioiodide was studied on 14 dogs. Individual experiments lasted from 2½ to 13 hours. Three dogs had total gastric pouches with an intact neurovascular supply, and 11 dogs were used in acute experiments. In the latter the stomach of the anesthetized animal was exposed surgically and severed from the duodenum and esophagus. Secretion of acid gastric juice was stimulated by food, or by intravenous or subcutaneous injection of histamine, insulin, or pilocarpine; alkaline gastric juice was evoked by stimulation of the greater curvature through arterial injection of acetylcholine(6). The animals were given a single intravenous injection of 20 to 200 microcuries of radioiodide,† with enough ordinary sodium iodide to raise the initial blood level to 10^{-2} to 10^{-1} millimol per liter. The carrier iodide was added in order to minimize sources of experimental error which may be caused by adsorption of the isotope on the equipment used, and to stabilize the serum iodide levels. One hundred microcuries of iodide consisting only of the isotope I^{131} weigh about 8×10^{-7} mg(7). Presumably, this amount of inorganic iodide would disappear rapidly from the serum through mechanisms such as removal by the thyroid or conversion to organic iodo compounds(8,9). Chemical determinations and

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radioactivity assays were done on individual fractions collected generally over 30-minute periods. Blood samples were withdrawn by venipuncture during the first half hour after the injection of radioiodide, at the end of the experiment, and at various intermediate periods. For radioactivity measurements, 0.2 ml of the liquid to be assayed was evaporated on an aluminum planchet. Sodium bicarbonate was added to the gastric juice samples to neutralize free acid and to raise their solid content to that of the serum. An end window tube was used for counting and the customary corrections were applied. The assays were reproducible to within ±10%, so that the biological variations encountered exceeded the error involved in the assays by a factor of 10. The iodide levels in gastric juice and serum were calculated on the assumption that the specific activity of the iodide in the serum and gastric juice was the same as that of the administered iodide(9). To the extent that the body iodide may have diluted the administered labeled iodide, the iodide levels thus calculated will be low.

Results and Discussion. We found iodide to be concentrated in gastric secretions with pH values ranging from 1 to 8, and irrespective of the secretagogue employed. In 2 experiments, in which an alkaline secretion was produced initially with acetylcholine and then changed to an acid secretion by injection of histamine, the isotope level in the gastric juice remained appreciably higher than the isotope level in the serum throughout with no significant change coincident with the fall in pH. Within individual experiments as well as among different experiments the gastric juice iodide levels showed wide fluctuations. We believe that these fluctuations may, at least in part, be due to wash out effects. Gastric juice levels considerably in excess of the serum levels persisted even after several hours of continuous secretion, and there was no fall in the concentration ratios at the end of prolonged experiments. Therefore, the concentration phenomenon cannot be ascribed to an initial high tide of radioiodide in the serum, which manifests itself in the gastric secretion later on.

The most significant results of our study are shown graphically in Fig. 1. Plotted on the ordinate are the values for iodide concentrations in the samples of gastric juice, divided by the concurrent iodide concentrations in the serum (concentration ratios). Plotted on the abscissa are the corresponding rates of secretion, in ml/30 min./kilo body weight of the dogs. The data were obtained from 226 specimens of gastric juice with varying pH values, collected in 14 experiments. Different methods of stimulation seemed to influence the secretion of iodide only to the extent that they affected the rate of flow of gastric juice. However, only samples secreted after the first half hour following the injection of iodide are included in the graph, because in most experiments the iodide level in the gastric juice secreted during the first half hour was lower than in subsequent specimens. It is evident from the graph that the concentration ratios of iodide for gastric juice, at constant low serum iodide levels, do bear a relationship to the rate of gastric secretion. High concentration ratios were generally obtained at low rates of secretion and the opposite also held true. Thus our findings differ from the statement of Davenport that "the concentration (of iodide) in the gastric juice is independent of the rate of secretion of the juice." The distribution of the data on the graph suggests that the relationship between the concentration ratios and the rates of secretion may follow an equation of the type $xy = \text{constant}$. This would imply that the amount of iodide which enters the gastric juice per unit time, at constant serum iodide levels, is constant.

Our incidental observations on the dependency of the gastric juice iodide level on the serum iodide level tend to confirm Davenport's findings. However, in individual experiments a drop of as much as 50% in the serum iodide level was not necessarily accompanied by a corresponding drop of the gastric juice iodide level. Only when experiments were compared in which the serum iodide levels differed by a factor of 5 or more

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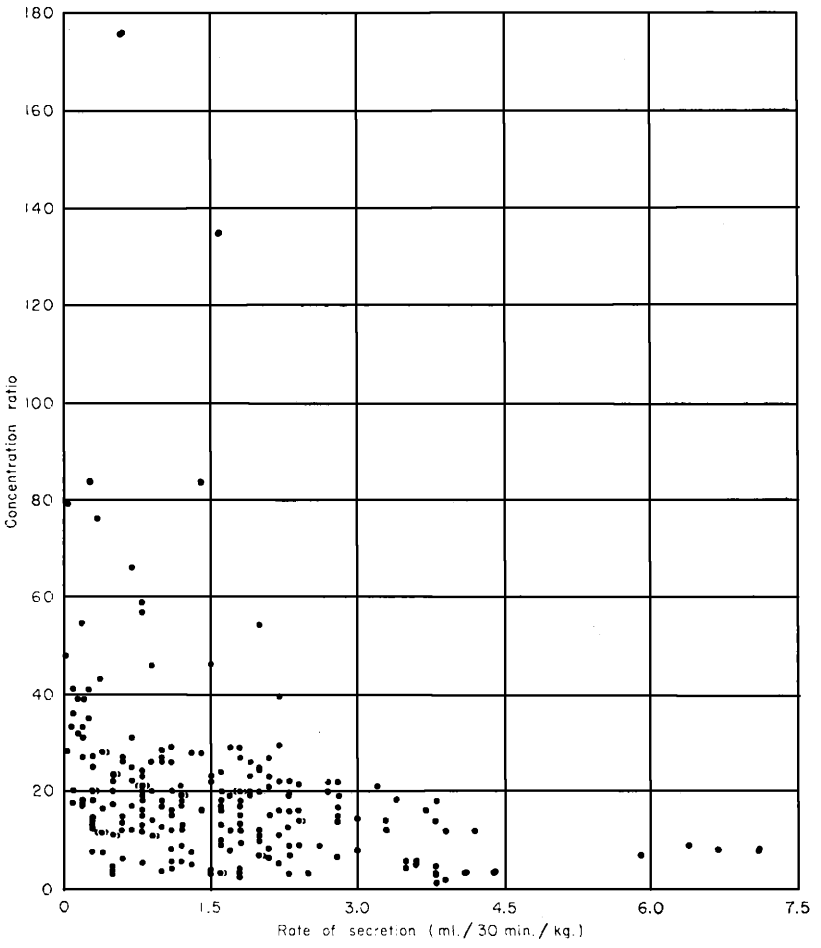

FIG. 1.

Relationship between concentration ratios of iodide for gastric juice and rates of gastric secretion.

did it become evident that the higher serum iodide levels resulted in an elevation of the gastric juice iodide levels. As was mentioned above, about half an hour was required at the beginning of most experiments before the initial rise in the gastric juice iodide leveled off. This may indicate that at least under our experimental conditions, about one-half hour is required before the serum iodide level manifests itself in the gastric juice. We have therefore recalculated some of the concentration ratios using serum iodide levels which prevailed approximately one-half hour prior to the collection of the gastric juice sample. The concentration ratios calculated in this manner are somewhat lower than the corresponding ratios given in the graph. However, since the serum iodide levels fell off rather slowly and uniformly, the distribution pattern of the values in the graph is not changed significantly. In any case it appears that a steady state between the iodide levels in the gastric juice and serum was never established. This is indicated by the comparatively slow rise of the iodide level in the gastric juice following intravenous injection, by marked fluctuations in gastric juice levels seen during the present study, and by the finding of Eisenman(10) that iodide enters the body fluids from the gastric contents very slowly.

No evidence was found to indicate that

radioiodine was present in the gastric juice in any form other than inorganic iodide. The isotope could be removed quantitatively from the secretion as palladium iodide, and paper partition chromatography(11) showed that the radioactive moiety in the secretion had the same R_f value as inorganic iodide. Extensive studies on the chemical forms in which radioiodine may be present in the serum have been carried out by other workers(12,13,14). It may be presumed that the isotope was present largely as inorganic iodide in the serum in our experiments. Any physicochemical binding of the injected iodide to components of the serum, or any conversion to organic iodo compounds, would render the serum iodide concentrations calculated from the radioactivity levels fictitiously high, and the corresponding concentration ratios fictitiously low. Corrections for the difference in the total solid content of gastric juice and serum would have the opposite effect, but would operate to reduce the concentration ratios by only about 10%.

The fact that iodine was concentrated in alkaline as well as acid gastric juice suggests that the secretion of acid by the parietal cells may not be necessary to bring about the concentration phenomenon. In an experiment on a dog with 4 divided pouches (prepyloric, lower body, upper body and fundus) iodide was found to be concentrated to about the same extent in the secretion from each pouch. Reports in the literature show that iodide is concentrated in gastric juice even in the presence of severe pathological changes in the gastric mucosa, such as linitis plastica(15) or carcinoma of the body of the stomach(16,17,18). Thus it appears that iodide can be concentrated from any region of the stomach, and that the concentration effect can persist even when the mucosa is physiologically and morphologically abnormal.

Summary. The secretion of iodide in acid and alkaline gastric juice at low serum iodide levels was studied in pouch dogs using radioiodide as a tracer. The concentration of iodide in the gastric juice was found to be independent of the pH of the gastric secretion, but it was influenced by the rate of gastric secretion. High concentration ratios for iodide were obtained at low rates of secretion and low concentration ratios at high rates of secretion.

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