Gastric Iodide and Chloride Clearances in Dogs.* (22835)

G. L. HOWELL† AND L. VAN MIDDLESWORTH
Department of Physiology, University of Tennessee, Memphis.

Inorganic iodide is concentrated in gastric juice of experimental animals(1-4) and human beings(5-8) as effectively as in the thyroid gland(9). Investigation into the mechanisms was complicated by injection of sodium iodide(1,2) which partially interfered with the iodide-concentrating process(1). Several authors(1,2) have suggested that iodide might replace chloride in gastric juice but investigations regarding secretory drugs(3,4) have not included quantitative chloride and iodide data that would test the possible interchange of iodide and chloride.

Plasma clearances of iodide by the stomach have been determined in patients(8) and in rats(10). The iodide and chloride clearances were considered satisfactory quantitative indices of gastric secretory mechanisms. The present investigations were undertaken to compare these functions under the influence of substances known to alter the iodide trap of the thyroid gland(11). It was considered that clearance studies might give a basis for comparison of iodide and chloride secretory mechanisms of the stomach and some comparison of the gastric and thyroid iodine trapping mechanisms.

Methods. Acute experiments with Nembutal anesthesia: Mongrel dogs were fasted 6-18 hours before the experiment. They were lightly anesthetized by intraperitoneal injection of 1 cc 5.5% Nembutal per 5 lb. The femoral veins were exposed on both sides, one for injections and the other for blood sampling. The stomach was exposed by a midline incision, the esophagus tied with strong cord, and the pylorus cannulated by tying into place a thick rubber tube introduced into the stomach through the duodenum. Then 15 to 90 μc of I^{131} were injected intravenously. After a 10-30 minute period for mixing, the stomach was washed with approximately one liter of warm water in 3-4 portions and then returned to its normal position in the abdomen. After 7.5 minutes a blood sample was taken and after 7.5 additional minutes the stomach's secretions were collected by washing with a liter of water in 3 or 4 equal portions. This procedure was repeated in order to have 2 control collections after which the animal was injected with either Histamine (3 mg), NaSCN (75 mg/kg), NaI (60 mg/kg), or acetazoleamide (Diamox, .5-1 g). After 10-30 minutes, the stomach was washed and 2 collections of gastric secretions made and a blood sample taken at the mid-time of each. The gastric secretions and blood were analyzed for I^{131} by scintillation counting. Chloride was determined mercurimetrically(12). Gastric iodide and chloride clearances were determined as follows: $\frac{\text{Gastric } I^{131} \text{ or chloride/min.}}{\text{Plasma } I^{131} \text{ or chloride/cc}}$. *Chronic experiments on unanesthetized dogs with Heidenhain or innervated total gastric pouch:* The dogs were fasted 18 hours preceding the experiment, and allowed water *ad libitum*. A venous blood sample was drawn preceding the experiment and analyzed for radioactivity to determine residual activity left from previous experiments. If activity was found, PBI^{131} was determined; this never exceeded 3% of the total plasma I^{131}. Ten to 40 μc of I^{131} were injected into the left leg vein. After a 30 minute period for mixing and equilibration, the pouch was washed with 200 to 300 cc of warm water, using 60 cc washing. Seven to 8 minutes later a blood sample was taken from the right leg and at 15 minutes a gastric collection was made by washing the stomach with 200 cc of water in 60 cc portions. After the 2 control collections, the dogs were injected with Histamine (3 mg), NaSCN (75 mg/kg), $NaClO_4$ (15 mg/kg), NaI (60-100 mg/kg) or reserpine (.25 mg/

* The study was supported by research grants from the USPHS and USAEC. The gastric pouches were prepared through cooperation of Dr. E. H. Storer and his staff of Department of Surgery.

† USPHS Medical Student Fellow.

TABLE I. Gastric Clearance of Iodide and Chloride.

Procedure	No. of exp.	Gastric clearance of plasma, cc/min. Iodide	Chloride
	Acute exp., Nembutal anesthesia		
Control	6 (3 dogs)	4.7 (2.4-7.5)*	.40 (.17-.67)
Sodium iodide, 60 mg/kg		.53 (.28-1.0)	.35 (.13-.61)
Control	4 (2 ")	3.4 (3.0-4.3)	.46 (.33-.74)
Thiocyanate, 75 "		.39 (.32-.41)	.26 (.20-.30)
Control	8 (4 ")	7.3 (4.3-10.2)	.27 (.12-.46)
Histamine, .1-.14 "		9.9 (7.3-12)	.66 (.24-1.3)
Control	6 (3 ")	4.2 (3.1-5.3)	.26 (.16-.32)
Diamox, .5-1.0 g		4.9 (2.9-6.4)	.24 (.15-.30)
	Unanesthetized female Heidenhain pouch dog		
Control	2	5.4 (4.8-6.0)	.27 (.21-.34)
Sodium iodide, 60 mg/kg		.70 (.60-.80)	.12 (.10-.14)
Control	2	4.4 (4.1-4.7)	.11 (.10-.12)
Thiocyanate, 75 "		.25 (.25-.45)	.12 (.10-.15)
Control	2	1.5 (1.3-1.6)	.12 (.11-.14)
$NaClO_4$, 15 "		.11 (—)	.12 (.11-.12)
Control	2	4.5 (4.4-4.5)	.10 (—)
Histamine, 3 mg		12 (11-14)	1.2 (.94-1.5)
Control	2	5.2 (4.8-5.7)	.25 (.24-.26)
Serpasil, 2.5 "		12 (9.5-14)	.87 (.57-1.2)
	Male Heidenhain pouch dog		
Control	2	5.4 (4.6-6.3)	.10 (—)
Na I, 100 mg/kg		.40 (.37-.42)	.08 (—)
Control	2	2.8 (2.6-3.0)	.08 (—)
NaSCN, 75 "		.32 (—)	.08 (—)
Control	2	3.2 (3.1-3.3)	.10 (.09-.11)
$NaClO_4$, 15 "		.13 (.12-.14)	.11 (.10-.12)
Control	2	5.5 (4.3-6.7)	.09 (—)
Histamine, 3 mg		25 (23-27)	1.7 (1.5-1.9)
	Male total innervated pouch dog		
Control	2	6.7 (6.4-7.0)	.19 (.15-.23)
NaI, 60 mg/kg		1.4 (1.1-1.6)	.15 (.12-.18)
Control	2	12 (9.4-14)	.27 (.25-.29)
NaI, 100 "		.90 (—)	.14 (.13-.15)
Control	4	4.3 (2.9-6.2)	.17 (.15-.19)
NaSCN, 75 "		.7 (.37-.80)	.16 (.09-.23)
Control	4	4.8 (3.4-6.8)	.20 (.12-.34)
$NaClO_4$, 15 "		.36 (.27-.54)	.21 (.13-.33)
Control	4	1.5 (1.0-2.7)	.24 (.17-.42)
Histamine, 3 mg		11 (9.0-13)	2.6 (1.7-3.3)

* Range; if no range stated there were 2 identical values.

kg). After a 30 minute period for mixing and equilibration, the pouch was washed and 2 15-minute experimental gastric collections made. Blood samples were taken at the mid-time of each. These specimens were analyzed for gastric clearance of chloride and I^{131} in the same manner as the samples from the acute experiments.

Results. Table I shows the control gastric I^{131} clearances varied among dogs and on the same dog from day to day. Control gastric I^{131} clearances varied from 1.5 to 11.7 cc plasma/min. The control gastric chloride clearances were 0.1 to 0.46 cc plasma/min., *i.e.*, 2% to 12% as great as the control iodide clearances. NaI administration depressed I^{131}

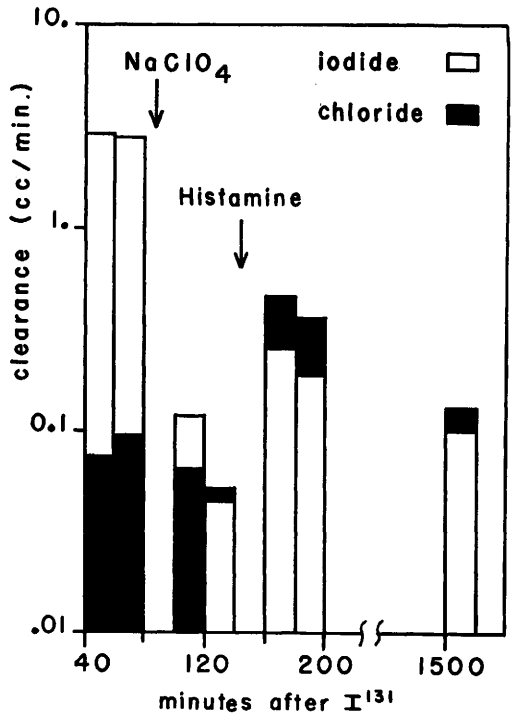

FIG. 1. Alterations in simultaneous iodide and chloride clearances of Heidenhain pouches. Each value represents an avg from 2 dogs. After each drug ($NaClO_4$ and histamine) one 20-min. collection was discarded without analysis.

clearance until it approached the chloride clearance. NaI did not cause as great a decrease in chloride clearance but there was the suggestion of a consistent reduction following iodide administration. NaSCN reduced gastric I^{131} clearance similar to NaI with no effect on chloride clearance except in the anesthetized dogs (Table I). $NaClO_4$ in 1/5 the dose of NaSCN produced the most severe reduction in I^{131} clearance which fell consistently to the level of chloride clearance. In these doses $NaClO_4$ produced no effect on chloride secretion. A single dose of perchlorate continued to exert maximum depression of gastric iodide clearance for more than 2 days in 3 dogs so studied.

Histamine produced a 10 to 18 fold increase in gastric chloride clearance in conscious dogs and 3 to 7 fold increase in the gastric I^{131} clearance.

In 2 dogs (Fig. 1) histamine was injected after demonstration of the $NaClO_4$ effect. The gastric chloride and iodide clearances then showed similar histamine responses.

Serpasil, used in 2 experiments on one dog, doubled the gastric I^{131} clearance and tripled the gastric chloride clearance. The Serpasil depressed the animal, and death occurred 3 days after the experiment. Diamox had no effect on basal chloride or I^{131} secretion.

Discussion. Apparently this is the first quantitative determination of the gastric I^{131} clearance in dogs. The results show: (1) those substances which greatly reduced the secretion of iodide by the gastric mucosa had little or no effect on the basal secretion of chloride, (2) histamine and reserpine produced a greater percent rise in the gastric chloride clearance than in iodide clearance, (3) the basal chloride clearance was only 2 to 12% of the basal iodide clearance, (4) when iodide secretion was blocked by a substance known to inhibit the thyroidal iodide trap, the gastric iodide clearance approached or reached the basal chloride clearance values. These data suggest that there are possibly two mechanisms for the secretion of iodide by the stomach, one that specifically traps iodide and rapidly secretes it, another non-specific mechanism in which iodide and chloride are interchangeable. This non-specific process was stimulated by histamine and not readily blocked. The specific process was effectively inhibited by elevated plasma iodide and by NaSCN or $NaClO_4$, similar to the iodide trap of the thyroid gland. Previous investigators who administered NaI probably blocked this specific iodide trap. The effect of $NaClO_4$, NaI, and NaSCN on the I^{131} clearance is possibly due to the anions of these salts combining with a specific system necessary for the transfer of iodide across the gastric cell. For normal function, this specific iodide trap may require an unsaturated carrier.

Histamine in absence of perchlorate (Table I) increased iodide clearance an average of 4 fold in unanesthetized dogs. Histamine in presence of perchlorate (Fig. 1) resulted in a similar (5 fold) increase in iodide clearance. Comparison of absolute results in gastric pouch dogs illustrates a dissimilarity between effects of histamine before and after

perchlorate. Before $NaClO_4$ injection, histamine increased the iodide clearance an average of 12 cc/min. but after $NaClO_4$, the increase was less than 1 cc/min. Therefore, the effects of histamine before and after perchlorate were relatively similar but absolutely quite different. This suggests that histamine had some effect upon the specific iodide trap of the stomach.

Summary. Iodide and chloride clearances were determined in anesthetized and unanesthetized dogs. The control gastric iodide clearance was 10-50 times greater than the chloride clearance. The iodide clearance could be 95% suppressed by anions known to block the thyroid iodide trap but chloride clearance was practically unchanged. In the presence of the blocking agent, gastric iodide and chloride clearances were similar. These data suggest at least 2 mechanisms for gastric secretion of iodide: (a) a specific iodide secretory system and (b) a non-specific mechanism in common with chloride secretion which continues to function after blockade of (a).

1. Davenport, H. W., *Gastroenterology,* 1943, v1, 1055.
2. Lagergreen, B. R., *ibid.,* 1950, v14, 558.
3. Mason, E. E., and Bloch, H. S., PROC. SOC. EXP. BIOL. AND MED., 1950, v73, 488.
4. Reugamer, W. R., *Arch. Biochem. and Biophysics,* 1953, v47, 119.
5. Honour, A. J., Myant, N. B., and Rowlands, E. N., *Clin. Sci.,* 1952, v11, 447.
6. Myant, N. B., *et al., ibid.,* 1950, v9, 405.
7. Schiff, L., *et al., J. Clin. Invest.,* 1947, v26, 1196.
8. Oeff, K., Kessel, M., and Krentz, K., *Klin. Wschr.,* 1955, v33, 59.
9. VanderLaan, J. E., and VanderLaan, W. P., *Endocrinology,* 1947, v40, 403.
10. Brown, Josiah, *ibid.,* 1956, v58, 69.
11. Wyngaarden, J. B., Wright, B., and Ways, P., *Endocrinology,* 1952, v50, 537.
12. Hawk, P. B., Oser, B. L., and Sommerson, W. H., *Practical Physiological Chemistry,* P. Blakiston's Son and Co., Philadelphia, 1954, 13 ed., p626.

Received July 23, 1956. P.S.E.B.M., 1956, v93.

Frequency of Abortive Parthenogenesis in Domestic Turkey.*† (22836)

I. L. KOSIN AND HELEN NAGRA (Introduced by James McGinnis)
Department of Poultry Science, State College of Washington, Pullman.

Abortive parthenogenesis in the chicken has been demonstrated to occur in eggs laid by virgin hens(1,2). Parthenogenesis also occurs in the turkey(3-5) and most of this development is of abnormal type. The available cytological evidence(6) is that nuclei of such parthenogenetically developing tissue are diploid. Kosin(7,8), in the absence of evidence to the contrary, ruled out parthenogenesis as a major factor responsible for the presence of aggregates of "moribund" cells observed in germ discs of apparently infertile eggs from mated hens. Following the first report by Olsen and Marsden(3) on the occurrence of parthenogenetic development in the turkey, a more intensive study of the matter was undertaken.

Materials and methods. The period reported here covers 1952-1956. The eggs were produced by the College strain of Broad Breasted Bronze hens and by U. S. D. A. strain of Beltsville Small White hens. The hens had been separated from males since 10-14 weeks of age. Upon separation, the birds were brought into completely enclosed pens where they remained for the entire observation period. Because the pens lacked windows, a low intensity artificial light (less than 1-foot candle power) was provided until the birds were 28 weeks old. At that time, the light intensity was increased to more than 5-foot candle power to stimulate oviposition.

* Scientific Paper No. 1515, Washington Agric. Exp. Stations, Pullman. Projects No. 803 and 1190.

† This investigation was supported, in part, by funds from Biological and Medical Research by State of Washington Initiative No. 171 and by Federal funds for regional research under the Hatch Amended Act, and conducted at Washington Agric. Exp. Station.