Secretion of Gastric Parietal Cells

The exact nature of the secretion of the gastric parietal cells is still debated[1]. While applying a new histochemical method it was found that the parietal cells secrete large amounts of a weak polyacid[2]. The present report deals with further investigation on this secretion following histamin stimulation.

Materials and Methods. Four mongrel dogs were fasted for 24 h and given sodium pentobarbital in doses sufficient to keep them sleeping during most of this period. Repeated doses of 5 mg diethylaminoethyl-benzilate-methobromide[3], were given intramuscularly during 6 h preceding operation. This premedication was maintained in order to produce prolonged inhibition of gastric secretion[4]. At operation the ligated stomach was incised and the pH of the gastric contents determined by indicator paper; biopsy specimens were then taken. Subsequently 0·7 to 1·0 mg of histamin hydrochloride was introduced into the peritoneal cavity, and the testing for acidity and taking of biopsies at half hourly intervals were carried out 2–3 times thereafter.

The biopsy specimens were fixed in Carnoy's fluid, embedded in paraffin and sectioned at 6 microns. They were stained with haematoxylin and eosin and by the Bi-Col method[2], which involves the use of 2 colloidal metal solutions. The colloidal iron is used in order to stain and block the strongly acidic groups, followed by staining with colloidal gold, which can now only react with the remaining weakly acidic compounds. Some series of sections were stained by the P.A.S. method, by the Ninhydrin-Schiff and the Million methods.

Results. The reaction of the gastric contents before histamin administration was neutral. 30–60 min later the reaction became acid (pH 1–4). Concomitant with the change in secretion, the Bi-Col method revealed changes in the appearance of the glands, which were similar in all the dogs but most clear in the dog from which the microphotographs of Figure 1 were taken.

In all the biopsy specimens blue-staining material (indicating strongly acidic groups, i.e. mucus) was found in the surface epithelium, in the foveolae and in the necks of the glands. In the first specimen (Fig. 1*A*, reaction neutral) dark brown material, indicating a high concentration of a weak acid, was found in the uppermost part of the glandular lumen and in a few parietal cells in this region. In the second specimen (Fig. 1*B*) the appearance was essentially similar. In both these specimens all the microscopical fields revealed the same picture. In the third biopsy taken 1 h after histamin stimulation (Fig. 1*C*, pH around 2) dark brown material was found in the lumina of the middle and upper parts of some glands. It was also found in some parietal cells, lying apparently within the cytoplasm or in the intracellular canaliculi. In the 4th specimen (Fig 1*D*, pH 1–2), the dark brown material was found along the entire length of the lumina as well as in most parietal cells. It may be noted that in the last 2 specimens areas were found which did not differ markedly from those observed in the first 2 specimens.

In P.A.S.-stained preparations there was diffuse staining of the parietal cells and of the secretion within the lumina. No appreciable staining of the described material was observed in Ninhydrin-Schiff and Millon stained preparations.

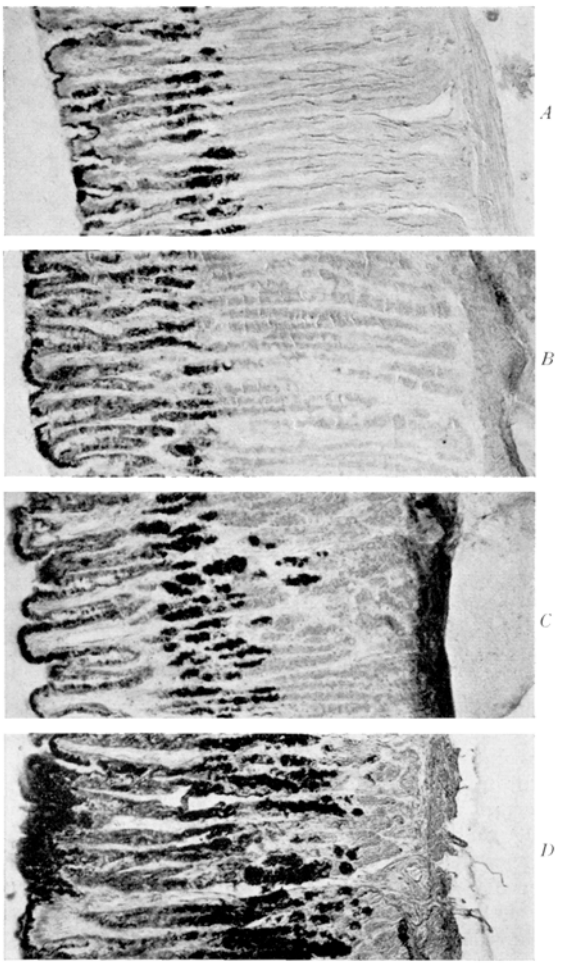

Fig. 1. Consecutive biopsy specimens of gastric mucosa of a dog. Bi-Col stain, × 120. Mouths of the gastric glands are to the left; here the dark staining material is mucus which is colored blue by the Bi-Col method. Dark staining material within the glands is mucoid which is stained dark brown by the same method.

Fig. 1*A*. First biopsy taken after long anaesthesia and administration of a ganglion blocking agent. Mucosa apparently at rest (reaction of gastric contents neutral), with dark brown granules in the uppermost parts of the glands.

Fig. 1*B*. Second biopsy, taken $^1/_2$ h after administration of histamine. Appearance of mucosa similar to *A*. (Reaction of gastric contents neutral.)

Fig. 1*C*. Third biopsy, taken 1 h after histamine administration. Dark brown material is present also in the middle portion of the glands, both in the lumina and in the parietal cells. (Reaction of the gastric contents acid; pH about 2.)

Fig. 1*D*. Fourth biopsy, $1^1/_2$ h after histamine stimulation. Dark brown material is present throughout glands in lumina and parietal cells. (Reaction of gastric contents acid; pH 1–2.)

Discussion. These findings indicate that the gastric parietal cells of the dog stimulated by histamin contain and secrete a substance which is demonstrable by the Bi-Col method. In apparently resting glands the substance is present only in the upper parts of the glands, where it borders on the mucus plug.

The material is obviously insoluble in the organic solvents used for fixation and embedding and apparently does not diffuse to a great extent during fixation. Previous

[1] E. J. CONWAY, *The Biochemistry of Gastric Acid Secretion* (C. C. Thomas, Springfield, Ill., 1953).

[2] M. WOLMAN, Bull. Res. Council Israel *6E*, 27 (1956).

[3] 'Paragone' Teva, Jerusalem.

[4] D. BIRNBAUM, Gastroenterologia *82*, 225 (1954).

(unpublished) experiments have indicated that it is moderately soluble in water. The intense staining with gold in the Bi-Col method (no other tissues in the body stain as intensely as this substance) indicates that it contains a very high concentration of weak acidic groups. The known fact that the parietal cells are acidophilic indicates that the net charge of these cells is positive; this probably implies that they contain numerous basic groups It has been shown previously[5] that the parietal cells stain intensely by treatment with OsO_4 in carbon tetrachloride, which might also indicate that they contain abundant hexosamine moieties. From the solubility characteristics it may be surmised that the substance is not a lipid and from other tests that it contains little if any protein and is probably of a saccharidic nature.

Material of identical staining characteristics was found in the parietal cells of human and rat stomach when the specimens were fixed in Carnoy's fluid within a short time after death. In 2 instances of gastric achylia in patients with pernicious anaemia (one of them being in remission), no such substance was found in the glands of the body of the stomach.

It may be recalled that HOERR and BENSLEY[6] reported on the presence of highly viscous material secreted by the parietal cells. It is surmised that the weak polyacid which stains with Bi-Col might be a precursor of HCl. The nature of the ion exchange which is probably involved in the secretion of HCl and the reason for the low organic content of parietal cell secretion need further study. A possible relationship between the weak polyacid and the intrinsic factor has not been investigated.

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Zusammenfassung

Parietalzellen aus Hundemagen sezernieren ein Polymer mit schwach sauren Gruppen, das mit der Bi-Col-Methode dargestellt werden konnte. Der Zusammenhang des Sekretes mit der Salzsäureproduktion wird diskutiert.

[5] M. WOLMAN, Exp. Cell. Res. *12*, 231 (1957).
[6] N. L. HOERR and R. R. BENSLEY, Anat. Rec. *56*, 417 (1936).

Über das Verhalten der optischen Isomeren von Adrenalin im Blut

Die teilweise Demethylierung, welche razemisiertes Adrenalin *in vivo* erfährt[1], und die unterschiedliche biologische Wirksamkeit seiner optischen Isomeren weisen auf ein von einander abweichendes Verhalten im Stoffwechsel hin.

Zur Abklärung dieser Frage wurden Katzen L- und D-Adrenalin infundiert und während der Infusion Adrenalin und Noradrenalin im Plasma fluorimetrisch bestimmt[2].

Diese Versuchsanordnung gestattet, die Abbaugeschwindigkeit des infundierten Stoffes zu messen und den Anteil Noradrenalin, der daraus gebildet wird, zu erfassen. Beim raschen Adrenalinabbau im Blut wird eine konstante Adrenalinkonzentration bereits nach wenigen Minuten erreicht (Plateau). Durch Demethylierung aus infundiertem Adrenalin gebildetes Noradrenalin erreicht wie dieses ein Plateau. Unphysiologisch hohe Adrenalinmengen wurden deshalb infundiert, um die Gleichgewichtskonzentrationen beider Pressoramine deutlich messbar über die Normalwerte zu heben. Gleichzeitig kann damit eine mögliche Grenze der Konzentrationsunabhängigkeit der Zerfallskonstanten ermittelt werden.

Das Verhältnis der Plateau-Konzentration von Noradrenalin zu derjenigen von Adrenalin ergibt den Anteil der Demethylierung (= Konversion) an allen Abbaureaktionen des Adrenalins unter der Voraussetzung gleicher Abbaugeschwindigkeiten für das primäre und das sekundäre Amin, wie sie in [1] gefunden wurden.

Die Ergebnisse dieser Versuche, die 180 Einzelanalysen der beiden Pressoramine im Plasma erfassen, sind in den Tabellen I und II wiedergegeben.

Aus Tabelle I geht hervor, dass nach Infusion von L-Adrenalin die Konzentration von Noradrenalin im Plasma ansteigt, und zwar im Mittel auf mehr als den halben Wert des Adrenalinplateaus. Im Gegensatz dazu erhöht eine D-Adrenalinzufuhr die Noradrenalinkonzentration nicht (Tabelle II). Die Zerfallskonstanten λ sind für beide Isomere im Mittel dieselben; sie betragen etwa 0,5 min^{-1}, das heisst der Adrenalinabbau geht mit einer Halbwertszeit von durchschnittlich 80 s in diesen Infusionsversuchen vonstatten. Dieser Wert ist 2–3mal höher als das Mittel aus Abklingkurven und vorläufigen Dauerinfusio-

[1] W. A. HUNZINGER, G. RITZEL und H. STAUB, Helv. chim. Acta *39*, 2096 (1956).
[2] H. WEIL-MALHERBE und A. D. BONE, Biochem. J. *51*, 311 (1952). – H. WEIL-MALHERBE und A. D. BONE, Lancet *1953*, 974.

Tabelle I
Dauerinfusionen von L-Adrenalin an Katzen. Alle Konzentrationen sind auf Plasma bezogen. Noradrenalinwerte korrigiert für Analysendefizit

Katze Nr.	Infusion μMol/l min	Adrenalin μMol/l		Noradrenalin μMol/l		λ_L min^{-1}	Konversion
		vor Infusion	Plateau	vor Infusion	Plateau		
3	0,44	0,016	0,51	0,027	0,48	0,86	0,9
4	0,375	0,003	0,57	0,017	0,098	0,65	0,1
5	0,515	0,003	0,84	0,060	0,23	0,61	0,2
11	0,65	0,011	1,5	0,018	0,36	0,44	0,2
12	0,345	0,024	0,79	0,086	0,38	0,44	0,4
13	0,63	0,012	3,8	0,016	4,5	0,17	1,2
14	0,58	0,013	1,2	0,13	0,77	0,50	0,6
15	0,24	0,020	0,60	0,095	0,73	0,40	1,2
Mittel:	0,47	0,013	1,22	0,056	0,94	0,51 ± 0,07	0,6 ± 0,16