Histamine Stimulation of Gastric Pepsin and Hydrochloric Acid in Patients of Vitiligo

SHUKLA and MUKERJI[1] observed that patients of vitiligo secreted subnormal amount of hydrochloric acid in the gastric juice. To find out how they responded to histamine stimulation, fractional gastric analysis was conducted in fifteen normal healthy individuals and thirty patients of vitiligo after subcutaneous injection of 0.01 mg of histamine acid phosphate/kg of body weight. Gastric secretions, aspirated every 5 min by syringe for 2 h, were later made into hourly volumes. In these hourly samples, free acid was found by titration against $N/10$ NaOH using phenolphthalein and Topfer's reagent as indicators, and pepsin was determined by GLICK's[2] modification of ANSON's[3] method using casein as the substrate. Hourly rate of output of free acid and pepsin was calculated from these volumes and concentrations.

The result was recorded in the Table.

The Table shows that both patients and normal subjects secrete 7–10 m.Eq. of hydrochloric acid/h. This amount of hydrochloric acid produces an approximate pH range of 2–3[4]. According to HOLLANDER[5], maximum conversion of pepsinogen to pepsin occurs at a pH range of 2–4.5. Therefore, at 2–3 pH, as observed in the experiment here, a maximum amount of pepsinogen would be changed to pepsin. Under these ideal conditions for formation of pepsin, it is found that patients of vitiligo are secreting two-thirds of the amount of pepsin to that secreted by the normal group.

The reduced value of enzyme in the stomach of patients will affect the hydrolysis of injested protein molecule at the more centrally located peptide linkage of α-carboxyl group of dicarboxylic amino acid and α-amino radical of aromatic amino acid[6]. The enzyme specifically splits this form of the peptide linkage which is present in L-tyrosine and L-phenylalanine residues[7]. Therefore, the deficiency of pepsin will interfere with the release of these amino acids. The action of the enzyme is quantitatively proportionate to the amount of pepsin[8], hence its lack will ultimately lead to a deficiency of amino acids phenylalanine and tyrosine. Phenylalanine is an essential amino acid[9] and along with tyrosine these form the basic substances for synthesis of melanine[10].

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Clinical category	No. of cases	Hourly output					
		Pepsin (Casein units)			HCl (m. Eq.)		
		Range	Mean	Median	Range	Mean	Median
Normal subjects	15	1920–51520	29039	34320	1.6–20	8.36	7.00
Vitiligo patients	30	1440–38400	21784	23020	0 –15	7.00	6.85

Therefore, it can be postulated that deranged synthesis of melanine in patients on vitiligo is induced by lack of secretion of pepsin. Detailed account of the work will be published elsewhere.

Zusammenfassung. Die stündliche Pepsinsekretion bei dreissig Vitiligo-kranken und 15 gesunden Personen wurde nach Histaminstimulation gemessen. Bei den Vitiligo-Kranken wurden zwei Drittel der normalen Pepsinsekretion beobachtet.

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[1] R. C. SHUKLA and B. MUKERJI, Ind. J. Med. Res. *48*, 714 (1960).
[2] D. GLICK, *Methods of Biochemical Analysis* (Interscience Publishers, N.Y. 1954), Vol. 2, p. 345.
[3] M. L. ANSON, J. gen. Physiol. *22*, 79 (1953).
[4] M. BROADANSKY, *Introduction to Physiological Chemistry* (John Wiley & Sons, N.Y.) IV. Ed., p. 18.
[5] F. HOLLANDER, Amer. J. Med. *13*, 453 (1952).
[6] M. BERGMANN and J. S. FRUTON, J. biol. Chem. *117*, 225 (1940).
[7] J. S. FRUTON and M. BERGMANN, J. biol. Chem. *127*, 627 (1939).
[8] M. BERGMANN and J. S. FRUTON, in *Advances in Enzymology* (Ed. F. F. HARD and C. H. WERKMAN, Interscience Publishers, N.Y. 1941), Vol. 1, p. 63.
[9] M. WOMAC and W. C. ROSE, J. biol. Chem. *107*, 499 (1934).
[10] H. S. RAPER, Biochem. J. *21*, 89 (1927).
[11] Thanks are due to Mr. R. K. SORAUT for his valuable assistance in this work.

The Influence of Reserpine upon the Changes in Femoral Blood Flow Produced by Stimulation of the Lumbar Sympathetic Chain[1]

The depletion of the norepinephrine stores in the heart[2–4] and in artery walls[5,6] is the likeliest explanation for the diminution of the characteristic response of the heart[7–9] and vessels to stimulation of adrenergic nerve fibers observed after pretreatment with reserpine. Recently graded doses of reserpine were found to cause a graded reduction in the effect of sympathetic nerve stimulation on myocardial contractility[9]. As an extension of these findings, the present study was designed to determine the relationship between reserpine dosage and function of the sympathetic nerves supplying the femoral vascular bed of the dog.

Under pentobarbital anesthesia and after 5 mg/kg heparin i.v. a double cannulation was made in the left external iliac artery of 18 dogs (7.1–14.8 kg). Blood from the proximal cannula was led through a Shipley-Wilson rotameter and back into the distal cannula. The perfusion pressure was measured from a sidearm placed just before the distal cannula. A sidearm placed just before the flowmeter was connected to the right external jugular vein so that, in order to lower the perfusion pressure, blood could be shunted away from the leg at will. The lungs were ventilated artificially with air. A thermometer was placed between the toes and the temperature was kept at

[1] This work was supported by grants from the U.S. Public Health Service H-2205, the American Heart Association 59-G-11, and the Eugene Higgins Trust.
[2] A. CARLSSON, E. ROSENGREN, Å. BERTLER, and J. NILSSON, in *Psychotropic Drugs* (Elsevier Publ. Co., Amsterdam 1957), p. 363.
[3] O. KRAYER and M. K. PAASONEN, Acta physiol. scand. *42*, Suppl. 145, 88 (1957).
[4] M. K. PAASONEN and O. KRAYER, J. Pharmacol. *123*, 153 (1958).
[5] J. H. BURN and M. J. RAND, Lancet *273*, 1097 (1957).
[6] J. H. BURN and M. J. RAND, Brit. Med. J. *1958* i, 903.
[7] U. TRENDELENBURG and J. S. GRAVENSTEIN, Science *128*, 901 (1958).
[8] S. HUKOVIC, Brit. J. Pharmacol. *14*, 372 (1959).
[9] J. R. BLINKS and D. R. WAUD, J. Pharmacol. *131*, 205 (1961).