—General Lectures—(I)

(1) CLINIDAL STUDY ON GASTRIN-METABOLISM

S. YAMAGATA, A. ISHIMORI, H. SAKURADA, M. SHIMOYAMA,
Su. YAMAGATA, and Y. MIURA
Prof. S. Yamagata's Dept. of Int. Med. Tohoku University School of Med., Sendai

Radioimmunoassay of gastrin using two antibody system revealed that fasting plasma level tends to be higher in renal disease 421 ± 329 than in cases of normal gastric mucosa (163.7±80.73 pq/ml) and other clinical entities. It was also found that the elevation of gastrin level in fasting plasma depends on the type of renal disease and the degree of functional disturbance of the kidney. Namely, it was seen that the advancement of renal dysfuncion expressed by the abnormal values in GFR, BUN etc. tends to accompany the elevation of gastrin level in fasting plasma in chronic nephritis, whereas the high level of fasting plasma gastrin was observed in patients of nephrotic syndrome with normal to only slightly disturbed renal function. The use of artificial kidney was found to lower the plasma gastrin level in patients with various degree of renal failure.

In order to clarity the role played by the kidney in gastrin metabolism, the plasma gastrin level was compared between renal artery and vein during the continuous intravenous administration of synthetic human gastrin I to the dog. Namely, about 32% of gastrin disappeared during the passage through the kidney which was influenced by blood pressure. However, only below 0.2% of administered gastrin was recovered in urine immunologically.

These findings were interpreted as that the kidney occupies the important position in the active gastrin metabolism and the disturbance of this function leads to the elevation of plasma gastrin level.

(2) A STUDY BY RADIOIMMUNOASSAY OF GASTRIN

O. KONDO, K. IMAMURA, Y. NAMEKI, and S. OMATA
Yokohama City Hospital Dept. of Med.
M. ABE
Hiratsuka City Hospital
T. SUYAMA
Keio Health Consultation Center, Tokyo

Measurement of intrinsic gastrin in different diseases, using gastrin-antidody, made according to Mcguigan method, is reported.

(**Method**) Antibodies to gastrin were obtained from rabbits after immunisation with human gastrin I which has been coupled to bouvine Serum-albumin by carbodiimide condensation. Three months old, male, New Zealander white rabbits were used. The gastrin-albumin solution containing 1.74 mg of synthetic human gastrin was mixed with 0.64 ml of Phosphate buffer solution and 0.16 ml of the adjuvant, and 0.2 ml of the mixture was injected into each limb of the rabbits.

The injection was reported 2 months later and 3 months thereafter. Serum was obtained 14 days after the third injection from the vein of the ear.

Confirmation of the antibody was performed by Ouchterlony agar gel diffusion method, using veronal buffer (pH 8.8) and a distinct precipitin line between BSA and antiserum was obtained. Each 2 μg of SHG was labelled with 2.2 mCi of I^{125} and purified by Sephadex G-10. The specific activity was 312 μCi per μg gastrin. Radioimmunoassay was performed by a double-antibody method.

The gastrin level was found to be 1.67 ± 0.54 ng/ml in normal controls, 1.65 ± 0.75 ng/ml in patients with peptic ulcr, 2.46 ± 0.87 ng/ml in patients with nephritis and 2.64 ± 0.72 ng/ml in patients with cirrhosis. In cases with cirrhosis it was clearly elevated 30 min. after the test meal. Our findings are slightly higher than those reported from abroad, and the temperature at the time of centrifugation and the condition in which the samples are preserved are being investigated as possible causes of the difference.

(**Conclusion**) 1. We obtained highly active antibodies to gastrin from rabbits throughi m-munisation with SHG.

2. The standard curve of 10^2 ng sensitivity was obtained, using highly active, I^{125}-labelled SHG and antisera diluted

3. Gastrin level was 1.67 ± 54 ng/ml in normal controls and elevated in nephritis and cirrhosis.

(3) RADIOIMMUNOASSAY OF GASTRIN (VII): RESPONCE OF PLASMA GASTRIN TO DRUGS AFFECTING AUTONOMIC NERVOUS SYSTEM

T. YAMAMURA*, H. OHKURA**, T. KITAMURA*, and M. SAKODA**

*; *Project Team for G. I. Hormone Research, Graduate School, Division of Medicine, Kobe University.*

**; *The Second Department of Internal Medicine, Kobe University, School of Medicine., Kobe*

Plasma immunoreactive gastrin (P. I. R. G.) was measured in rabbits before and after 2, 5, 10, 20, 30, 60, 90 and 120 minutes I. V. administration of drugs affecting autonomic nervous system. The influences to P. I. R. G. of some other drugs were also examined. α-stimulating agent, Methoxamine 1 mg/Kg I. V. caused moderate but temporary increase of P. I. R. G. after 2 to 5 min., while Phentolamine 0.5 mg/Kg, as α-blocking agent, decreased P. I. R. G. from just after I. V. administration to about 30 min. β-stimulating agent, Isoproterenol 20 μg/Kg increased P. I. R. G. and maintained this high level till about 60 min. or more. Propranolol 25 μg/Kg, as β blocking agent, caused early temporary increase of P. I. R. G. but tendency of slight decrease was observed after 10 to 60 min. Acetylcholine 1 mg/Kg increased P. I. R. G. after 10 min. but rather decreased after 30 to 60 min. Atropine 50 μg/Kg caused slow increase of P. I. R. G. after 10 to 120 min. These results may suggest not only parasympathetic system but also sympathetic system or such-like system affects secretion of gastrin.

Histamine decreased P. I. R. G. after 2 to 30 min. but slightly increased after 30 to 120 min. Secretin 5 Boots Units/Kg decreased P. I. R. G. remarkably just after administration and lasted low level after 120 min. or more. The administration of dibutyl cyclic A. M. P. 10 mg/Kg I. V. made almost no change of P. I. R. G. level as 0.9% NaCl. Parathyroid hormone 20 U. S. P. Units/Kg caused early but slight increase (2 to 5 min.) and decrease (20 min.). Thyrocarciton in 20 M. R. C. Units/Kg I. V. decreased P. I. R. G. after 2 to 60 min., while acidity of gastric juice decreased from 10 to 90 min. (peak: 30 min.)

These results may give us very interesting problems and keys to think the mechanism of gastrin and gastric secretions.