GASTRO-INTESTINAL HORMONES

喬治・華盛頓大學醫學院　醫科校友　蕭逸夫

At the turn of this century, Bayliss and Starling (1902) suggested the existence of a humoral control of pancreatic secretion. However, their suggestion was sharply criticized. The thinking of physiologists at that time was so strongly based by the extensive and outstanding work on reflex action that it was impossible to get prompt acceptance of this completely revolutionary concept. Later on more convincing evidence was reported, and since then the concept has been accepted. The study of humoral control on the gastrointestinal tract has attracted many investigators. Early work was done with crude gut extracts. Due to the impurity of the preparation, the physiological functions were controversial. Depending on the function of the preparation, different hormonal names were derived. There was always a question as to whether the preparation studied by one group of investigators was similar to that studied by the other groups. At the end Of the 1950's, progress in technology made it possible to isolate the pure components of the extracts. The functions of these purified hormones could then be investigated in detail. Suprisingly enough, many hormones which had been thought to be different entities turned out to be a single hormone having a broad spectrum of action. So far, the structure of three gastrointestinal hormones have been elucidated. These are gastrin, cholecystokinin, and secretin.

GASTRIN:

Gastrin has been isolated from the antral mucosa of four species: namely, man, dog, hog, and sheep (Grossman, 1967). In all of these species gastrin has an essential peptide chain containing 17 amino acids. In these animals gastrin has been found to occur in two forms, gastrin 1 and gastrin 11. The latter has an ethereal sulfate on the ring of tyrosine in position 12. Although these two gastrins have different physicochemical properties, they appear to have similar physiological function. Gastrin has been shown to be produced by the mucosa of the pyloric gland area of the stomach, but the cell which produces gastrin has not been identified.

The spectrum of action of gastrin is suprisingly broad; it is a strong stimulant f

gastric acid secretion and for pancreatic enzymes secretion. It is also a weak stimulant for pepsinogen secretion from the stomach and bicarbonate secretion from the pancreas. In addition, the rapid injection of large doses of gastrin results in contraction of the smooth muscle of the stomach, small intestine, colon, and the gall bladder (Emas and Grossman, 1967). Since the dose used in this experiment was well beyong the physiological range, the possible physiological role is not established.

The active site of gastrin is the C-terminal tetrapeptide amide, Try-Met-Asp-Phe-NH_2. This fragment produces the entire spectrum of action of the whole molecule but is only about one fifth to one tenth as active on a molar basis. Lengthening the tetrapeptide amide by adding the amino acids that comprise the N-terminal portion of gastrin causes a uniform increase in potency for all the physiological actions (Grossman, 1967, 1969).

CHOLECYSTOKININ (PANCREOZYMIN):

Cholecystokinin is identical to pancreozymin in structure (Jorpes, 1968). Since cholecystokinin was discovered first, this term, cholecystokinin, will be used hereafter. This hormone is a very potent stimulant for the secretion of pancreatic enzymes Cholecystokinin and gastrin have an identical C-terminal pentapeptide amide, Gly-Try-Met-Asp-Phe-NH_2, and therefore have essentially the same spectrum of action. However, at some sites cholecystokinin is the more potent hormone, whereas at other sites gastrin is (Grossman, 1969).

For the greatest efficacy cholecystokinin requires the C-terminal heptapeptide amide, Try-Met-Gly-Try-Met-Asp-Phe-NH_2. Desulfation of the molecule results in a marked

HSO_3

decrease in all actions. The higher the potency of cholecystokinin for a given action, the greater is the decrease caused by desulfation (Jorpes, 1968, Grossman, 1969). One of the most striking features of lengthening the heptapeptide amide chain is the decrease in its potency. This is the only known example in a biological system where a fragment of a molecule has a higher potency than the whole molecule.

SECRETIN:

Secretin was the first gastrointestinal hormone to be discovered. It has been demonstrated that secretin is released into the portal circulation in the presence of acid in the duodenum and the jejunum. The actual site of secretion is not identified, but it is known to be in the villi or from villus epithelial cells. Secretin stimulates the secretion of water and bicarbonate from the pancreas and has no effect on enzyme secretion. The structure of secretin has also been elucidated. Although the active site has not been identified, at least 27 amino acids appear to be required for the action of the molecule (Jorpes, 1968).

In addition tothe well recognized hormones, many other hormones have been reported

in the literature. Among these, enterogastrone, incretin, duocrinin and intestinal gastrin have been suggested to be a mixture of two or more of the already known gastrointestinal hormones. Hormones such as villikinin, enterocrinin, and antral cholane have also been reported, but neither the chemical structure nor the physiological function of these reported hormones has been verified. Further studies might provide new information concerning the structure and function of these reported hormones.

REFERENCES:

Bayliss, W.M. and Starling, E.H.
The Mechanism of Pancreatic Secretion
J. Physiol. 28: 325-353, 1902

Ems, S. and Grossman, M.I.
Differences in Responses Between Dogs and Cats to Large Dose of Gastrin on Gastric Secretion
Gut 8: 267-275, 1967

Grossman, M.I.
Some Aspects of Gastric Secretion
Gastroenterology 52: 882-892, 1967

Grossman, M.I.
A Resume of a Lecture Given at The Annual Meeting of Gastrointestinal Society of American Physiological Society. Atlantic City, N.J.
April 17th, 1969

Jorpes, J.E.
The Isolation and Chemistry of Secretin and Cholecystokinin
Gastroenterology 55: 157-164, 1968

作者蕭逸夫爲本學院醫科第一屆畢業校友，

民國五十六年獲美國喬治華盛頓大學的"**Fellowship**"，

於今年四月廿八日通過論文考試而榮獲**Ph. D**學位，

綠杏所有同仁願在此致最大賀忱。