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SIR JOHN GADDUM

Four days before this Symposium started, J. H. Gaddum died at the age of 65 after a long illness uncomplainingly borne. His pharmacological interests being centred around biologically active tissue constituents, he made many valuable contributions in the field of catecholamines. His earliest paper in 1926 was on the interaction of adrenaline and ergotamine; it was a quantitative study of the phenomenon and demonstrated the laws governing this interaction. In 1933, Gaddum, together with Schild, was the first to use fluorescence in alkaline solution to estimate adrenaline in solution, a reaction which forms the basis of later fluorescence techniques. Five years later there followed, in collaboration with Kwiatkovski, the discovery that ephedrine in low concentrations sensitizes organs to the action of adrenaline, whereas high concentrations are inhibitory. Theories to account for these actions included that of competition with receptors to explain inhibition. In this, and in subsequent papers, Gaddum was trying to identify the transmitter released from the rabbit's ear on nerve stimulation, and correctly concluded that it probably was adrenaline. In contrast, he suspected noradrenaline to be the so-called sympathin E released from nerves to the liver, and his work with Goodwin, interrupted as a result of the war, stated that this view is compatible, but not convincingly proved, by the experimental results. A few years later, Peart in Gaddum's laboratory was the first to demonstrate the release of noradrenaline on stimulation of sympathetic nerves.

This result was based on preceding work by Gaddum and co-workers, in which the specificity of bioassay was greatly improved by using parallel tests on a number of isolated organs, and by calculating the errors involved in such methods. A further advance was the discovery of the method of "superfusion" by which the sensitivity of certain bioassays is greatly enhanced. In 1957, Gaddum, with M. Holzbauer, wrote a monograph on adrenaline and noradrenaline; his last paper on catecholamines appeared in 1958, when he and Krivoy studied the excretion of these substances after the administration of reserpine. His report at the first catecholamine symposium was on "bioassay procedures."

M. VOGT

NILS-ÅKE HILLARP

Nils-Åke Hillarp was born in 1916. He defended his thesis at the Medical Faculty of the University of Lund, Sweden, in 1946 and then served as assistant and associate professor there. From 1960 to 1962 he was given a position by the Swedish Medical Research Council, that enabled him to devote himself entirely to research at the Department of Pharmacology, University of Götheborg. In 1962 he was given a call to the chair of histology at Karolinska Institutet, Stockholm. He held this position till his death on March 17, 1965.

Hillarp's three main scientific contributions have all been of great importance for the research field to which the present Symposium was devoted. In his now classical thesis he was able to clarify the structural organization of the peripheral innervation apparatus of the autonomic nervous system. Earlier speculations of a syncytial organization were disproved, and it was shown that the innervation apparatus consists of discrete fiber systems with its terminals converging onto the effector cells. Hillarp's conclusions met with considerable resistance initially but have received strong experimental support from subsequent work by himself and others and are now generally accepted.

Hillarp started out as a morphologist, but already in his early work his interest in functional aspects is apparent. His subsequent work was largely devoted to some fundamental problems in the field of neurohumoral transmission. In 1953 he—and independently Blaschko—discovered that the adrenal medullary hormones are stored in specific intracellular particles, and a few years later he and v. Euler showed that similar "storage granules" occur in adrenergic nerves. Subsequent work by Hillarp and his co-workers showed that in the storage granules a major fraction of the adrenal medullary hormones are held in complex form together with an equivalent amount of adenosine triphosphate (ATP) and an acid protein. In more recent work they—and independently Kirshner—discovered that isolated storage granules are able to incorporate catecholamines from the surrounding medium by an ATP-Mg^{++}-dependent mechanism which is specifically blocked by low concentrations of reserpine. Subsequent work has emphasized the functional importance of the storage granules and led to the concept that incorporation of the amines into the storage complex is essential for making them available for release by the nerve impulse.

Hillarp's third main contribution was to develop, in 1961 and 1962, a histochemical method permitting the visualization of catecholamines and 5-hydroxytryptamine in cells and nerve terminals under the fluorescence microscope. The reader of this volume will find that the discoveries emerging out of this work, carried on by Hillarp's enthusiastic pupils, represent one of the main events of this Symposium. It is true that this has not been one man's work, but to those who have had the opportunity to follow this fascinating development in all its details, it is clear that it was primarily the result of Hillarp's brilliant imagination, broad knowledge and experimental skill.

Hillarp was as great a personality as a scientist. His unusual generosity, warmheartedness and enthusiasm made his many friends and pupils love and adore him.

ARVID CARLSSON

ROSEMARY CASS

The death of Rosemary Cass, on May 16th last, at the age of thirty-three is a tragic loss. Her absence from meetings will be keenly felt, especially by her contemporaries who knew her as a friend and colleague.