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## Introductory Remarks (Second Day): Neurosecretion

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## Introductory remarks (second day): neurosecretion

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Our session today needs few words of introduction, for most of the foundations for our programme this morning have already been laid during the papers and discussions yesterday. It is perhaps only in relation to the secretory activities of neurons (which we shall discuss later this morning), and in particular the use of the term 'neurosecretion' that some comments of mine might be appropriate and useful.

For many years those of us who are interested in the field of neuroendocrinology have appropriated the word 'neurosecretion' to describe certain specific elements in the central nervous system which appear to be engaged in endocrine activity. The earliest of these specialized neurons to be described, namely those tracts linking the hypothalamus and pituitary pars nervosa in vertebrates, and those linking the brain and the sinus gland in crustaceans and the corpora cardiaca of insects, were clearly distinguishable by histological means from other neurons. Moreover, in terms of function and biochemistry also these classical neurosecretory systems seemed to have distinct characteristics. Unlike other neurons they released peptide hormones into the bloodstream and this, and some other features, formed the basis for the original neurosecretion concept proposed by Scharrer and Bargmann.

Today some of you may feel, as I do, that the dividing lines between those neurosecretory neurons, or, as Scharrer put it, 'neurones with glandular activity', and the adrenergic neurons with secretory activity which form the focal point of this meeting have become rather blurred. I can assure you that this problem has been for long a preoccupation of neuroendocrinologists—but especially in recent years as the findings of electron microscopy and biochemistry have revealed many resemblances between the classical peptidergic neurons of Scharrer and Bargmann and a number of aminergic systems.

Both types of neuron contain their secretory products in electron-dense, membrane-bound granules. In these granules a satellite protein accompanies the active principle; in peptidergic neurons, neurophysin—in aminergic neurons, chromogranin. Recent studies indicate that some of this satellite protein may be released with the active principle, in both types of neuron, though what this may mean in terms of function has yet to be determined.

The terminals of both peptidergic and aminergic fibres contain not only electron-dense granules but also smaller electron-lucent vesicles. Here again the role that these may play in release of an active principle has not yet been elucidated.

Constriction of either peptidergic or aminergic axons leads to a pile-up of stainable material on the proximal side of the ligature, thus denoting synthesis in the perikaryon.

At one time the considerable storage of stainable material in the distal portions of many neurosecretory axons was considered to be a diagnostic feature but, today, thanks to the fluorescence method of Falck and Hillarp we know that substantial storage of stainable material can also be demonstrated in adrenergic axons. Any differences in storage capacity between peptidergic and aminergic neurons would appear therefore to be quantitative rather than qualitative.

I have already drawn attention to the direct discharge by some neurosecretory neurons of their products into the bloodstream. For a while this seemed to distinguish these neurons from other elements of the c.n.s. Today this is no longer a valid distinction for we have found that some neurosecretory neurons make synaptoid contacts with intrinsic pituitary cells. Conversely, there are indications that some adrenergic neurons, notably in the median eminence, may exert effects at a distance by release of their products into the bloodstream.

Many neuroendocrinologists in recent years, faced by the difficulty of making a clear distinction between peptidergic and aminergic systems, have turned to a more broadly functional implication of the term neurosecretion. At the two most recent international symposia on neurosecretion both peptidergic and aminergic systems were discussed, their only common feature being that they were all directly or indirectly concerned in endocrine control. Thus support was given to a proposal made by Knowles and Bern, namely that the term neurosecretion should include all those neurons, whether peptidergic or aminergic, which have either a first degree endocrine activity, by the secretion of hormones into the bloodstream, or a second degree endocrine activity by their control of endocrine parenchyma. We recognize that this is, in a sense, an artificial boundary for convenience, and may be a transitory one. Yet by thus extending and yet delimiting the boundaries of the original neurosecretion concept, without altering the original endocrine concept of neurosecretion, we make possible the use of the term neurosecretion to denote all those elements which link the two great control mechanisms of the body—nervous and endocrine. Thereby some boundaries vanish, but others remain, and we see neurosecretion as one more aspect of what Dr Blaschko has described as the diversity within the unity of nervous structure and function.