PHARMACOLOGICAL REVIEWS
Vol. 24, No. 2

Printed in U.S.A.

Molecular Biology of the Sympathetic Nervous System

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THIS Symposium, sponsored by the New York Heart Association, is most timely and demonstrates the rapid advances that have been made in our understanding of the sympathetic nervous system. The discovery of chemical neurotransmitters was made early in this century but the identification of the sympathetic neurotransmitter, norepinephrine, was made only a little over 20 years ago. Its precursors and metabolites were identified even more recently. The enzymes involved in the biosynthesis and metabolism of the transmitter have received intensive study and most of them have now been purified and characterized. However, all this is not enough to tell us how the sympathetic nervous system functions. Some hints of regulatory processes in the sympathetic nervous system were presented at the Second Catecholamine Symposium in 1965 (3). Since then we have begun to recognize that sympathetic nervous activity is modulated by changes in the rate of synthesis and degradation of dopamine, norepinephrine and epinephrine. Regulation by end-product inhibition, allosterism, repression, and derepression, mechanisms which were first established in studies on microorganisms, are now known to play important roles in the sympathetic nervous system. We are also beginning to recognize the significance of the organization of the enzymes within the nerve cells with respect to their regulation and function. The participants of this Symposium will discuss current concepts of regulatory mechanisms in the sympathetic nervous system and present some of the experimental evidence on which these concepts are based. It will become evident during these discussions that newer technology, much of it derived from other fields such as immunology, fluorescence and electron microscopy, make possible these advances. Clinicians as well as laboratory scientists are now aware that the turnover of the catecholamines in tissues is of greater significance than the observed tissue concentrations.

It will also become apparent during this Symposium that we are no longer talking of one transmitter. Furthermore changes in nerve activity, produced by whatever mechanisms, result in changes in the rates of synthesis of these transmitters. Acute changes in nerve activity trigger one type of mechanism (1); chronic changes in nerve activity trigger another type (2, 4). Thus during short periods of exercise, hypotension (drug induced or endogenous) or decreased temperature, norepinephrine synthesis is increased. The onset of this type of increased synthesis is extremely rapid as is its disappearance when conditions revert to normal. Under such conditions no changes are observed in the amounts of synthetic enzymes in the tissues. When great demands are made on the sympa-

thetic nervous system, over long periods of time it responds by gradually increasing the levels of catecholamine synthesizing enzymes in the tissues. Conversely, in hypertension or under conditions where there is an increased production of catecholamines, levels of the synthetic enzymes in tissues may be diminished.

It has also been apparent for a long time that other hormones modify sympathetic activity. Some of these interactions can now be explained at the enzymatic level.

These newly discovered mechanisms may explain observed physiological and pathological responses. They may also explain the actions and limitations of some present day drugs and may make possible the development of new drugs. Although such new information is important in itself, it is obvious that it also has great practical value in clinical medicine. One can expect from it new advances in diagnostic and therapeutic procedures, particularly in cardiology, neurology and psychiatry.

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