SYMPATHETIC INNERVATION OF MURINE THYMUS AND SPLEEN: MORPHOLOGICAL AND FUNCTIONAL ALTERATIONS FOLLOWING CHEMICAL SYMPATHECTOMY

By

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SUMMARY

The thymus and spleen receive direct noradrenergic innervation to both perivascular and parenchymal elements. Although the density of parenchymal fluorescent fiber innervation is not as abundant as that seen in the salivary glands or the atria of the heart (Bjerre et al., 1975) it is certainly of sufficient magnitude to propose a major role for such innervation. It is proposed that norepinephrine is released from both the perivascular and parenchymal plexuses of nerve fibers and that it interacts with receptors on lymphocytes within the thymic parenchyma and the splenic white pulp. There is also the possibility that released norepinephrine modulates histamine release from mast cells in the thymic parenchyma. Noradrenergic varicosities can release norepinephrine at considerable distances from effector tissues (Lever et al., 1965), permitting the NE to diffuse through the surrounding adventitia (Su and Bevan, 1970). Norepinephrine levels in the splenic vein are higher than levels in the splenic artery suggesting that some norepinephrine can diffuse from its perivascular or parenchymal origin between the lymphocytes in the white pulp and into the open-ended splenic venous sinuses (Brown and Gillespie, 1957).

Evidence for specific receptors for neurotransmitters on lymphocytes, sympathetic innervation of lymphoid tissues, and alteration of immune responses _in vitro_ following exposure to neurotransmitters suggested that an _in vivo_ interaction could exist between the autonomic nervous and immune systems. Following histofluorescence demonstration of NE fibers in thymus and spleen, the extent of sympathetic innervation of thymus

and spleen was further studied and quantified by LCEC. The functional role of sympathetics on the humoral immune response to SRBC was probed by chemical ablation of peripheral sympathetics followed by immune testing. Six-OHDA and α-MT were both shown to be effective sympathectomizing agents, as verified by comparisons of experimental (sympathectomized) and control innervation patterns with histofluorescence, and by quantitation of catecholamines in experimental and control groups. Anti-SRBC-PFC responses were repeatedly significantly higher in 6OHDA treated mice when compared to controls. More complete sympathectomy, affecting both serum catecholamines and effector organ catecholamine levels, was achieved with 6OHDA + α-MT. This combined drug treatment resulted in a significantly increased anti-SRBC-PFC response when compared to 6OHDA alone treated experimental and saline treated control mice.

It is suggested that the sympathetic nervous system, composed of sympathetic innervation of lymphoid organs and augmented by plasma catecholamines of adrenal origin, has a suppressive modulatory role over the humoral immune response to SRBC. This neuromodulatory mechanism could act directly on developing and/or mature lymphocytes, or could act indirectly through modulation of histamine release from mast cells that are closely associated with sympathetic fibers in thymus and spleen. It is possible that immune responsiveness _in vivo_ depends in part upon a delicately blanced hormonal milieu in the thymus and spleen maintained by neurotransmitters provided by autonomic innervation of lymphoid tissue.

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