Calcium Homeostasis in Asthma

To the Editor:

The recent editorial, "Calcium channel antagonists in coronary artery spasm and bronchial spasm" by Robert G. Townley, (*Chest* 1982; 82:401) posed a variety of interesting issues. Inferred among them was the potential role of calcium homeostasis in bronchial asthma. In 1979, we[1] reported an increased sensitivity to extracellular calcium $(Ca^{++})_E$ in airways smooth muscle following *in vitro* anaphylaxis in the guinea pig. This post-anaphylactic acquired sensitivity to $(Ca^{++})_E$ was based upon the finding of an increase in resting isometric smooth muscle tension assayed in a Ca^{++}-free medium to which $(Ca^{++})_E$ was cumulatively restored. Preliminary experiments indicated that incubation in putative "anaphylactic" mediators was not the cause.[2] While the responsible cellular homeostatic mechanism is not defined, this work suggested: normal airway smooth muscle + anaphylaxis → acquired Ca^{++} defect (*eg* membrane) → sensitivity to $(Ca^{++})_E$ → increased basal muscle tone.

Since that time, other published observations have supported this concept. Measuring calcium efflux rate constants by the method of Hurwitz and Joiner,[3] Rodger and Martorana[4] found trachealis muscle from ovalbumin-sensitized guinea pigs to exhibit a definite change in the utilization and binding affinities of activator calcium. Similarly, employing Ca^{45} release from microsomal fractions of sensitized guinea pig lungs, Hedman[5] reported a small but statistically significant difference in Ca^{45} microsomal binding in comparison to control animals.

Collectively, these observations should be viewed as preliminary findings. They do nevertheless suggest some acquired defect or disturbance in Ca^{++} membrane flux or intracellular Ca^{++} homeostasis in airway smooth muscle following immunogenic activation since it appears well established that transcellular fluxes of calcium are critical in influencing basal cellular metabolism and cellular response to membrane stimulation. It may be of more than passing interest that such a primary disturbance of cellular calcium metabolism is also speculated to be an important factor in the pathogenesis of human and animal hypertension, implying a basic similarity in these two smooth muscle disorders. In asthma, a lability in Ca^{++} homeostasis could account for an alteration in the threshold to specific agonist contractile processes, as well as the effect of nonspecific processes which presumably must also increase free myoplasmic calcium to the contractile-regulatory processes in smooth muscle. Concurrently myorelaxation may also be affected. We believe the concept of a calcium-modulating defect could be fundamental to the genesis of human asthma.

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References

1 Weiss EB, Viswanath SG. Calcium hypersensitivity in airways smooth muscle: Isometric tension responses following anaphylaxis. Respiration 1979; 38:266-72

2 Weiss EB. Effect of anaphylactic mediators, acetylcholine and β-adrenergic blockage upon calcium hypersensitivity in airways smooth muscle (abstract). Am Rev Respir Dis 1980; 121-4:101

3 Hurwitz L, Joiner PD. Mobilization of cellular calcium for contraction in intestinal smooth muscle. Am J Physiol 1970; 218:12-19

4 Rodger I, Martorana MG. Excitation-contraction coupling in sensitized guinea pig airway smooth muscle. (Abstract) Fed Proc 1980; 39:296

5 Hedman SE, Andersson RGG. Studies of the contracting mechanism induced by slow reacting substance of anaphylaxis (SRS-A): Interaction with calcium. Acta pharmacol et toxicol 1982; 50: 379-84

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